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MALIGNANT NEOPLASIAS OF HÆMOPOIETIC AND CONNECTIVE TISSUES IN VARIOUS COUNTRIES

CANCER INCIDENCE IN DENMARK 1943 TO 1953 V.

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INTRODUCTION

It is the aim of this paper to present and analyze as detailed as possible the material of "Cancer registeret", the Danish Cancer Registry, on the incidence of malignant neoplasias of hæmopoietic and connective tissues, on the background of a review of corresponding information from elsewhere.

It has been realized in theoretical research, although perhaps not yet by the medical professions generally, that one malignant disease may be caused by a number of different etiological factors which also in the single case may replace each other wholly or partly, accumulating their carcinogenic effect. Thus, the significance in human pathogenesis of some factor suspect of carcinogenic effect, however well demonstrated in animal experiment such effect may be, can only be checked through statistical analysis of human cases, because the presence or absence of other carcinogens may influence results decisively, quite apart from the pronounced difference in "susceptibility" between species to various carcinogens. As an example we may mention the overwhelming importance of genetic factors to carcinogenesis in mice, to which no parallel of clinical importance has been demonstrable up to now.

Statistical research in cancer is, nevertheless, only inadequately equipped for meeting the requirements of this situation. The demonstration of widespread carcinogenic effects, like those of cigarette smoke, has proved feasible, but to demonstrate a possible additional effect of town smoke presents serious difficulties not to speak of the problems involved in a quantitative evaluation of the hypothetical interaction of such carcinogenic factors. These — inherent — limitations of medical statistics and their significance to the present situation may be illustrated with the example of C. M. Jespersen who first demonstrated a statistical correlation between general paralysis and syphilis in 1874, at a time when the technical demonstration of the causative agent was out of practical reach. At present the study of neoplastic diseases is at a corresponding stage. In fact, our first task will be to arrive at the demonstration of carcinogenic potency with reasonable certainty and within reasonable time. With this achievement in hand research will be able to leave statistics to the task of assisting public health officers in practical administration.

To this comes the fact that up to now leukæmias are so rare diseases that a number of publications on materials from whole countries have for lack of cases dealt with combined figures for the two sexes, or have for this and other reasons collected myeloid and lymphatic leukæmias in the same category. It is true that distinction between the two diseases is often difficult, but it has to be realized that differences in age distribution between the two diseases, and between men and women, will seriously narrow the statistical permissibility of summing them up for statistical purposes, since the basis of statistics is uniformity of material. For the evaluation of statistical publications in this field it is therefore necessary that the material is divided up as far as possible, for the reader to judge the justification of treating two different materials as one.

Statistical material on leukæmia, whether illustrating morbidity or mortality, is up to now of limited size but scattered in journals and reports of very different nature, so that the facilities for evaluating our knowledge on the occurrence of these diseases will be restricted to specialized institutes, at a time when such evaluation gradu-

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ally is becoming more important in view of the increasing exposure of Man to radiation. Contributing to this state of affairs is the fact that most medical journals are disinclined to publish in necessary detail those tables which alone will make it possible for readers remote in space or in time to evaluate the reality of differences between figures reported and the validity of conclusions drawn. Nevertheless, statistics are, so far, our only means of estimating carcinogenic effect in humans, and thus there may be some hope that more Editorial and other Boards may come to realize that special publication facilities are equally necessary to this branch of research as to radiology, histopathology or experimental pathology. Until this happens much material will be left unpublished, or as multiplied manuscripts, or printed only in governmental statistical reports.

Consequently, we have tried in the following to quote as fully as possible essential tables and diagrams dealing with the demographical aspects of leukæmia and allied diseases, from the relatively short period and the few regions from which a reasonable degree of accuracy may be expected. It follows that we have only included material of a truly demographical character, bearing on the incidence of these diseases among populations or well defined parts of populations, while surveys of hospital material have only been taken into consideration when derived from a delimited population of known size and age distribution. As an exception we have not been able to quote, except by a few diagrams, the extensive international material collected and published by the World Health Organization. Purely statistical publications have on the whole been regarded as less important, if not discussed medically from the region in question, and the same applies to tables and diagrams representing both sexes at one time.

Mortality statistics have formed the basis of most studies of this kind, and will provide us with important information as long as the diseases in question are invariably fatal. On the other hand it should be recalled that the diagnosis of hæmopoietic and allied neoplasias will require certain facilities which may not be demanding as far as most cases go, but will depend on the special attention of the doctor, if the case shall not pass under some obscure heading. Rare as these diseases are, such lack of attention may seriously invalidate the material of some regions, or even of some age groups.

Morbidity studies aiming at the determination of the number of new cases of malignant disease diagnosed within a given population during a certain period have in the last decades been undertaken in various countries as the United States or Denmark. It is obvious that incidence rates at various ages will be more accurate when based on the age at first diagnosis than when based on age at death, as in mortality studies, and also information on the elements of diagnosis will be available through studies on morbidity.

However, both methods will suffer from the dualism caused by difference in the basis of diagnosis between hospital cases and cases diagnosed in general practice. In some instances this dualism may be avoided through hospital admission of all cases, provided that this does not just mean that cases are never discovered except on hospital admission. It should be added that also the per cent of hospital admissions may sometimes vary with the age of patients, with fatal consequences to the statistical validity of the material, when this possibility is not taken into consideration.

It may not be superfluous to underline that while mortality studies on malignant diseases have often been carried out with considerable caution, so that conclusions drawn have been of lasting validity, as in the case of authors like Stern (1844), Walshe (1846) or Sibley (1859), incidence studies have already more than once led into loosely founded hypotheses, based primarily on the observation of parallelism between two statistical trends, but without any biological background. On the side of authors such hypotheses are most often meant as an inspiration to later workers, while in reality they often prove a time-consuming obstacle to conscientious research, demanding more trouble to refute than to advance.

In the present paper the new Danish material on incidence of leukæmia and allied diseases will be given separately. Like other national figures these should be judged not only on an international background, but also with a view to the interest taken in these diseases by the national medical profession.

Since Ellerman & Bang in 1908 transmitted fowl leukæmia by means of a cell-free filtrate, studies on leukæmia and other diseases of the hæmopoietic system have been continued in Denmark, favoured after some years by the generosity of the Anders Hasselbalch Fund, and later also by the Lady Tata Memorial Trust and other foundations. Schools of research developed around workers like Oluf Thomsen with his colleagues Engelbreth-Holm, Rothe Meyer and others who later were assisted by their own associates. In Aarhus research dates from the work of Krebs, Rask-Nielsen and Wagner, later continued by Bichel, Kieler and others. In the more clinical hæmatological field names like, Gram, Gormsen, Meulengracht, Petri, Plum and others represent series of papers round which individual publications of other workers are centered.

On this background it will be understood that new diagnostic methods will easily spread in a country of about four million, which may well be reflected in the statistical material presented in the following.

EARLIER DEMOGRAPHICAL STUDIES

Table 1.
(Gram & Nielsen)

Year	Deaths from Leukæmia and Pseudoleukæmia Denmark 1920–28 Leukæmia	Pseudo-leukæmia	Age	544 Leukæmia Deaths 3/12 to 84 years, distributed by age. Deaths Capital	Denmark excl. Cap.	Whole Country.
1920	43	7	0—9	7	66	73
1921	46	7	10—19	9	38	47
1922	56	7	20—29	18	37	55
1923	69	8	30—39	9	34	43
1924	48	7	40—49	17	51	68
1925	74	2	50—59	26	82	108
1926	72	2	60—69	27	80	107
1927	63	3	70—79	9	31	40
1928	73	1	80—89	0	3	3
Total	544	44	Total....	122	422	544

The first demographical study on leukæmia in Denmark was published in Danish by H. C. Gram & R. Nielsen (1932), but has repeatedly been quoted secondhand through J. Nielsen (1932). It dealt with death certificates from 1920 to 1928. The authors realized the serious shortcoming of their material through lack of specified diagnoses, since out of 544 cases, 120 were specified as lymphatic, 117 as myeloid and the remaining 307 were distributed with 66 in the group "acute", seven as "aleukæmic", while 234 were designated as "leukæmia" only. It is also pointed out that outside Copenhagen cases of mononucleosis and other diseases may have been included in the material.

Table 2.
(Gram & Nielsen)
Leukæmia Deaths According to Sex.

	Capital Total	Capital per cent	excl. Capital Total	excl. Capital per cent	Whole Country. Total	Whole Country. per cent
Men	77	63.1	235	55.8	312	57.4
Women	45	36.9	187	44.2	232	42.6
Persons	122		422		544	

Starting from the observations that leukæmia appeared to be rare among the well-to-do patients while pernicious anæmia was not infrequent in this group, Gram & Nielsen tentatively analysed the occupation of 325 men aged over 20 years who died from leukæmia, and found:

Unskilled labourers: 46; independant farmers: 61; sailors & fishermen: 5; country artisans: 21; skilled labour: 30; artisans & trade: 31; white collar: 16; officials: 13; liberal professions: 4; various and unknown: 8.

An attempt at computation of rates per million population would show 74 for typographers and 202 for keepers of restaurants and inns but only 40 for farmers and 14 for "immaterial activities".

In their geographical survey (see Table 3) the authors with caution point to the fact that Fjend's medical district showed 12 cases reported by 8 various doctors.

Table 3 a & b.
(Gram & Nielsen)

Area	Population 1925	Deaths Total 1920-28	Deaths Annual per Million
Whole Denmark	3,434,555	544	18
Rural areas	1,992,395	284	16
Towns	1,442,160	260	20
København City	587,150	122	23
Borough of Frederiksberg ..	104,209	22	23
Aarhus	76,226	16	23
Odense	52,376	11	23
Sjælland (excl. of København & Frederiksberg)	648,702	94	16
Fyen	339,654	55	18
Jylland	1,575,533	242	17
Lolland-Falster	133,631	12	10
Bornholm	45,676	1	2
Further:			
Fjends medical district	32,951	12	40
Holstebro med. dist.	28,358	1	4
Isle of Taasinge	4,277	4	104
County			
Københavns County (excl. of København & Frederiksberg	180,413	27	16
Frederiksborg County.....	113,075	15	15
Holbæk County	121,951	15	14
Sorø County	114,008	14	14
Præstø County	119,255	19	18
Svendborg County	145,804	24	18
Odense County	193,850	31	18
Vejle County	163,647	24	16
Skanderborg County	110,731	22	22
Aarhus County	139,377	32	25
Randers County	147,206	18	14
Aalborg County	178,382	19	12
Hjørring County	148,181	15	11
Thisted County	83,199	14	19
Viborg County	139,881	28	22
Ringkøbing County	151,801	22	18
Ribe County	136,695	25	23
South Jutland Counties	176,433	23	14
Bornholm County	45,676	1	2
Maribo County	133,631	12	10

Uddströmer (1934) collected all cases of lymphogranulomatosis verified histologically on biopsy or postmortem examination in Swedish units with expert assistance from 1915 to 1931. This period was chosen because an initial survey of the records from the Pathology Department of the Caroline Institute showed 1915 to be the first year in the present century with only slight tendency to increased frequency of Hodgkin's disease. Uddströmer's material comprised 555 cases of which 467 had been diagnosed by biopsy and 88 by autopsy. Seven cases had to be discarded. The author notes that the incidence of cases per annum increased about seven times during his period of observation to 0.11 per 10 000 in 1931: "This increase in incidence is probably to the greatest extent illusory, yet the possibility of real increase cannot be entirely excluded."

Table 4.
Relative Age Incidence in 536 Cases of L. G. with Known Age at Onset af Disease Expressed in Number of Cases on 10,000 living Subjects per Age group. (Uddströmer 1934, Sweden).

Years	Men	Women	Both sexes
0— 5	0.42	0.08	0.25
5—10	0.70	0.04	0.38
10—15	0.32	0.29	0.31
15—20	0.61	0.49	0.55
20—25	1.31	1.50	1.41
25—30	1.25	0.90	1.07
30—35	1.04	1.43	1.24
35—40	1.76	0.67	1.19
40—45	1.67	0.74	1.20
45—50	1.24	0.58	0.90
50—55	1.99	0.80	1.38
55—60	2.29	0.79	1.50
60—65	2.24	1.08	1.62
65—70	1.42	0.64	0.99
70—75	0.75	1.10	0.94
75—80	0.00	0.17	0.10
All Ages	1.09	0.68	0.88

The age distribution of Uddströmer's material has later been used by MacMahon (1957) in support of the assumption of a bi-modal age incidence curve for Hodgkin's disease. His quotation of the curve does not do full justice to its shape owing to the fact that the level is far below the curves for U. S. A. and Denmark from a later period quoted in the same figure. However, there seems to be no reason to doubt Uddströmer's assumption that many cases have been missed during the first part of his observation period and so the shape of the curve may well be left in some doubt.

Morton Levin (1944) who studied the incidence of malignant neoplastic diseases in Upstate New York, exclusive of New York City, for 1942, reported 447 cases of leukæmia, of which 253 new cases and 277 deaths. This paper does not contain information on age distribution.

Sacks & Seeman (1947) studied leukæmia death rates for the United States Death Registration States from 1900 to 1945 and give important information on the significance of the five revisions of the International List of Causes of Death during this period; it may be noted that prior to 1933, the death registration area did not encompass the whole United States.

Until the revision of 1920 only a single title, under which Hodgkin's disease was also classified, was assigned for leukæmia. It is impossible therefore to discuss mortality for leukæmia from 1900 to 1920 without recognizing the exaggeration inherent in the figures as a result of more os less closely allied conditions. With the revision of 1920 a subclassification for pseudoleukæmia was established to make possible the classification of Hodgkin's disease separately from true leukæmia. Relatively minor changes in specific terms under the rubric for true leukæmia had been made since 1920. In the discussion of leukæmia mortality in the United States since 1920, only the figures for true leukæmia were used by Sacks & Seeman.

It should be noted, however, that the omission of all deaths charged to pseudoleukæmia from 1920 to 1938 results in an understatement of the mortality from the leukæmic process. This fact was demonstrated in 1940 when a comparative analysis of deaths in that year classified under both the revision of 1929 and the revision of 1938 was made by the U. S. Bureau of the Census. This study revealed that in 1940, 2139 deaths would have been charged to the pseudoleukæmia title of the 1929 list. Of these deaths 1 777 or 83 per cent were due to Hodgkin's disease and 247 or 11 per cent were due to aleukæmia, which being in reality a form of leukæmia appeared to have constituted a significant proportion of the deaths attributed to the pseudoleukæmia title. Sacks & Seeman point out that since the entire rubric of pseudoleukæmia has been excluded from their study the figures from 1920 to 1938 will obviously err on the conservative side.

In the revision of 1938, currently in use when Sacks & Seeman made their study, the rubric for pseudoleukæmia was discontinued, and diseases so certified were classified under nonspecific diseases of the blood; a separate classification for Hodgkin's disease was provided in the residual group of communicable diseases, and a new subrubric for aleukæmias was established. To maintain continuity, only the leukæmia figures since 1938 were used by Sacks & Seeman, who estimate that problems of classification added to those of diagnosis and reporting result in an understatement of the number of deaths from leukæmia.

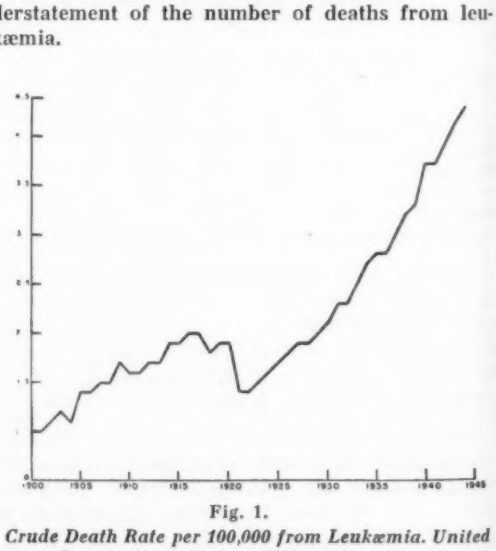


Fig. 1.
Crude Death Rate per 100,000 from Leukæmia. United States Registration States 1900—1944. (Sacks & Seeman).
"The apparent drop in the death rate in 1921 observed in fig. 1 results primarily from the revision of this title in 1920."

Sacks & Seeman give rates for White and Nonwhite U. S. citizens of which the specified part is quoted below. They conclude that white persons are affected at a rate more than twice as great as nonwhites, and that some of the differences must be attributed to variations in the availablity of diagnostic services. Males experience a rate approximately one-third greater than females.

Table 5.
(Sacks & Seeman)
Leukæmia Death Rate per 100,000 Population, by Race and Sex, United States Death Registration States, 1925—1940.

White		Nonwhite	
Male	Female	Male	Female
4.6	3.3	2.4	1.3
3.9	3.0	1.7	1.3
3.9	2.8	1.8	1.3
3.6	2.8	1.7	1.3
3.5	2.6	1.3	1.1
3.4	2.5	1.5	0.9
3.1	2.5	1.5	1.2
3.0	2.2	1.3	0.7
2.8	2.2	1.1	0.6
2.8	2.0	1.1	0.8
2.6	1.9	1.3	0.6
2.3	1.8	0.9	0.6
2.3	1.8	0.9	0.7
2.2	1.7	0.7	0.6
2.1	1.7	0.8	0.7
2.1	1.5	0.9	0.6

The study by Sacks & Seeman also comprises an international comparison reviewed later, and an analysis of a small material af 154 deaths from leukæmia from Baltimore 1939—1943. Data in their paper are presented with full consideration to the importance of distribution on race, sex, and age, etc., and the authors are fully aware that the increase in mortality rates for leukæmia cannot be accounted for by changes in the age distribution of the population, because the age-specific death rates had increased in each group. It is concluded that the factor of increasing recognition of the disease resulting from improved diagnostic facilities must be given adequate consideration.

Incidence of leukæmia in Denmark was first reported upon for the period 1942—44 by Clemmesen, Busk & A. Nielsen (1949) who gave incidence rates at various ages for each sex for 308 lymphatic and 198 myeloid cases of leukæmia together with 299 cases of Hodgkin's disease and 181 leukæmia cases of uncertain type. As far as 1943—44 is concerned this material is incorporated in the studies presented later in this paper.

Shimkin, Mettier & Bierman in 1951 published death rates for various ages for leukæmia in the U. S. Death Registration States for the years 1910, 1920, 1930, and 1940. These authors find that all data show a continually higher mortality of leukæmia, although it is not possible to establish whether this represents a true increase or is due to improved recognition and reporting. During the period 1910 to 1948

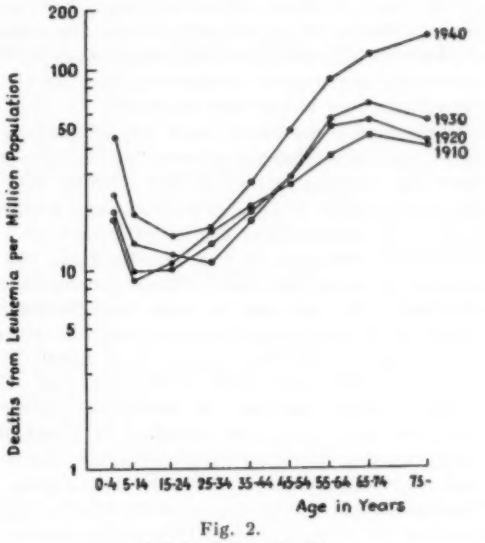


Fig. 2.
(Shimkin et al.)

they find a progressive and consistent shift in the sex ratio toward a higher proportion of females among patients with myelocytic and other leukæmias. Today it may be objected that such a change will be difficult to evaluate, because the age distribution of mortality rates as may be seen from Fig. 3 also in U. S. A. is different for myeloid and lymphatic leukæmia and for the sexes, so that changes in the age distribution of the general population may well cause a change in the sex ratio.

In 1952 Clemmesen, Busk & A. Nielsen had extended their material on Danish morbidity to cover the period 1942 to 1946. It now numbered: for myeloid leukæmia 215 men and 203 women, for lymphoid leukæmia 382 and 215, and for unspecified leukæmias 71 male and 61 female cases. Hodgkin's disease was represented with 222 men and 166 women. It appears from the age distribution of incidence rates for the whole country that curves for myeloid and lymphoid leukæmia and lymphogranulomatosis differed considerably in shape, but with no material from elsewhere for comparison, the authors abstained from further comments, since it was uncertain whether the shape of such curves might be local phenomena. Their figures for whole Denmark with per cent of hospital cases will be included in the total Danish material represented in the tables of the present paper.

The topographical analysis of the three authors demonstrated no variation in density for myeloid and lymphoid leukæmia, while lymphogranulomatosis showed a few irregularities. A statistical test indicated higher variations for myeloid leukæmia and lymphogranulomatosis than expected from theory. In particular the latter showed high incidence in the county of Thisted for 1942, notably

in the isle of Mors, while no cases had been notified during the entire period from the islands of Møen and Falster, but these differences do not prove any epidemical occurrence, and have not been confirmed in our present study.

Furthermore mortality rates for all leukæmia and lymphogranulomatosis were studied directly from the original tables of the Danish Health Service for 1931 to 1945, which in contradistinction to its publications are uninfluenced by the continuous changes in the international classification of deaths that have proved so troublesome elsewhere. No increase in rates was found for Hodgkin's lymphogranulomatosis and this disease showed identical crude rates for Capital, Provincial Towns and Rural Areas (cf. Fig. 15), while a slight increase in leukæmia mortality rates for both sexes was ascribed to diagnostic improvements following the introduction of sternal marrow puncture, which will have taken place in Denmark about 1937, corresponding with the statement of S h i m k i n et al. of 1935 as the year when this procedure was adopted in California. The authors made no comments at their finding of lower mortality rates 1931—1945 for total leukæmia in rural areas than in the capital, and rates for provincial towns between, but C l e m m e s e n & N i e l s e n (1952) confirmed it on the morbidity material from Cancerregisteret for 1943 to 1947 with age distribution of incidence rates for all leukæmia and for lymphogranulomatosis, while B u s k (1952) specified leukæmia types giving figures for all Denmark.

In his paper B u s k also reviewed the extensive material of V i d e b æ k (1947) who had compared the incidence of leukæmia among relatives of 209 leukæmia patients and 200 control persons. As demonstrated by B u s k the two groups show no difference if the study is limited to close relatives, the fate of which with regard to leukæmia will be equally well — or badly — known by the person questioned, whether or not a case exists in the family at the time of inquiry. Thus, we have to abandon the concept of leukæmia as a hereditary disease.

From 1949 figures were available for the United States on mortality from leukæmia and malignant neoplasms of the lymphatic tissues and reticuloendothelial system, and were presented by G i l l i a m (1953). Those of his tables that are specified on sex and give rates for various age groups are quoted as our Table 6—7 and Figures 3 and 4.

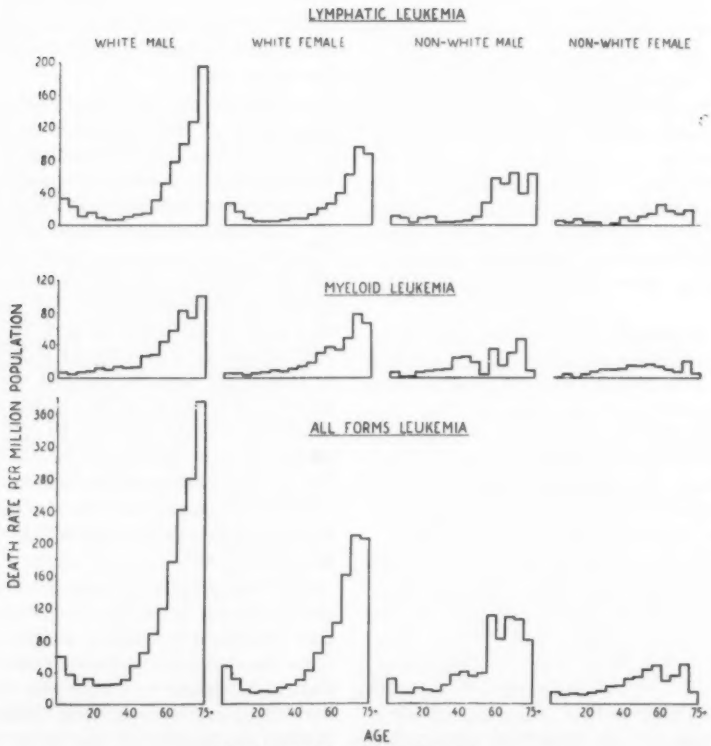


Fig. 3. (G i l l i a m redrawn).

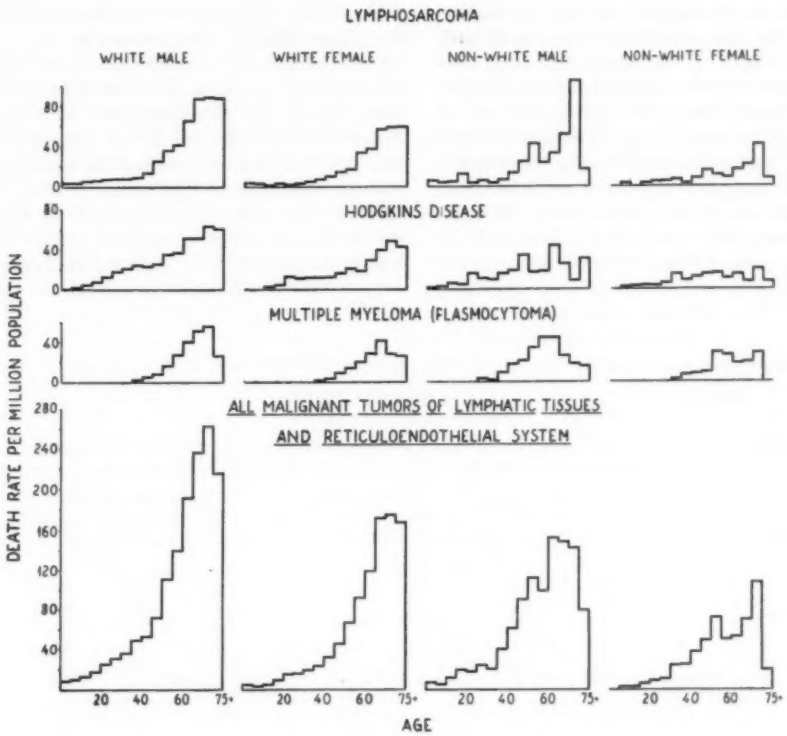


Fig. 4. (Gilliam redrawn).

Table 6—7 (after Gilliam).

Number of Deaths and Death Rates per 1,000,000 Population by Race and Sex for Deaths Attributed to Leukæmia and Neoplasms of the Lymphatic Tissues and Reticuloendothelial System in the United States, 1949.

	Number of deaths				Death rates per 1,000,000			
	White		Non-white		White		Non-white	
	Male	Female	Male	Female	Male	Female	Male	Female
Lymphatic leukæmia	1924	1235	100	53	29.12	18.45	13.03	6.59
Myeloid leukæmia	1395	1114	88	63	21.11	16.64	11.46	7.83
Monocytic leukæmia	252	180	11	11	3.81	2.69	1.43	1.37
Acute leukæmia, unspec. type	373	290	15	9	5.64	4.33	1.95	1.12
Other and unspec. leukæmia	509	407	38	35	7.70	6.08	4.95	4.35
All forms of leukæmia	4453	3226	252	171	67.39	48.20	32.83	21.26
Reticulum cell sarcoma	230	126	14	13	3.48	1.88	1.82	1.62
Lymphosarcoma	1346	875	92	41	20.37	13.07	11.99	5.10
Other neopl. of lymphoid tissues	221	154	15	8	3.34	2.30	1.95	.99
Hodgkin's disease	1414	908	100	54	21.40	13.57	13.03	6.71
Giant follicular lymphoma	13	9	—	—	.20	.13	—	—
Other forms of lymphoma (reticulosis)	279	208	17	6	4.22	3.11	2.21	.74
Multiple myeloma	567	458	68	43	8.58	6.84	8.86	5.35
Mycosis fungoides	26	17	3	3	.39	.25	.39	.37
Total (excl. leukæmia)	4096	2755	309	168	61.99	41.16	40.26	20.89

With a view to Hodgkin's disease mortality statistics from the United States were reviewed by Shimkin (1955). (Figs. 5 and 6). In consequence of the international classification for death registration between 1921 and 1938 there was an overstatement in the number of deaths classified under Hodgkin's disease, which during this period was listed under pseudoleukæmia and from 1939 under infectious diseases, while from 1942 to 1948 special tabulations available to Shimkin enabled him to reduce the hiatus to the period 1939—1941. The 1948 revision finally placed Hodgkin's disease under neoplasms.

Shimkin now found that from 1921 to 1938 the slopes of increase for leukæmia and for Hodgkin's disease are approximately parallel, but after 1942 the slope for the latter becomes less steep than for the former, which he ascribed to procedural classification changes. Between 1942 and 1951 the rate per million in the U. S. Death Registration States rose from approximately 40 to 60 for leukæmia and from 14 to 17 for Hodgkin's disease.

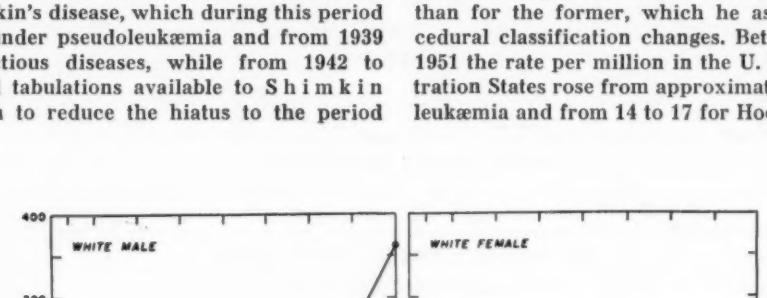


Fig. 5. (Shimkin) Leukæmia Death Rates, U. S. A.

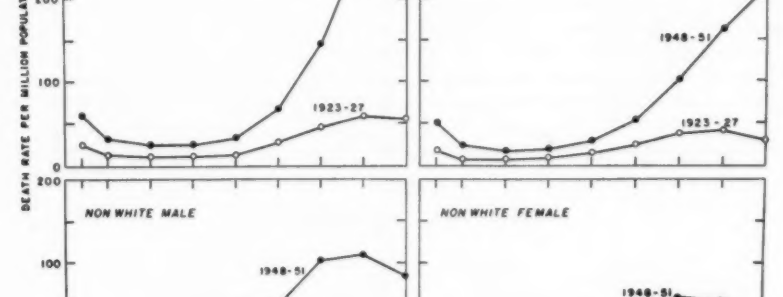


Fig. 6. (Shimkin) Hodgkin's Disease. Death Rates, U. S. A.

Distribution by race, sex and age is given in Figs. 5 and 6. It is remarkable that while the increase in rates for Hodgkin's disease is evenly distributed on all age groups, the increase for leukæmia is most pronounced among the old. Shimkin agrees with Sacks & Seeman that availability and acceptance of hospitalization and diagnostic procedures may be different for different age groups and races. He rightly finds that despite the continued increase in the *recorded* death rates a true rise in the incidence of leukæmia or Hodgkin's disease cannot be established.

Now, Griswold, Wilder, Cutler & Pollack (1955) reviewed morbidity material collected in Connecticut. From 1935 up to 1951, a period during which the population rose from 1.6 to 2.0 million, information had been collected from hospitals, and matched with case records, although only retrospectively as far as the period 1935—1940 incl. was concerned. Incidence rates at various ages are given for "acute" and for "chronic" leukæmia with rates for "lymphatic system generalized" and "hematopoietic system". Consequently, the possibility for comparison with other material will be limited only for the sites here treated.

Table 8.
(Griswold et al.)

Connecticut, 1935–51. Hematopoietic System. Average Annual Incidence Rates per 100.000.

	All Hematopoietic System			Chronic Leukæmia			Acute Leukæmia			Other Hematopoietic System		
	1935—40	1941—46	1947–51	1935—40	1941—46	1947–51	1935—40	1941—46	1947–51	1935—40	1941—46	1947–51
Age						MALE						
0— 4	3.4	5.1	5.4	—	—	—	2.6	3.6	4.2	0.9	1.6	1.2
5— 9	3.9	3.1	4.3	—	—	—	2.4	2.0	3.3	1.6	1.1	1.0
10—14	2.7	2.8	2.5	—	0.2	0.3	2.1	1.7	1.6	0.7	0.9	0.6
15—19	2.2	1.3	2.5	0.2	—	0.3	1.3	1.1	1.9	0.7	0.2	0.3
20—24	1.5	1.7	2.8	0.2	—	—	0.4	1.1	2.2	0.9	0.6	0.6
25—29	2.9	1.7	2.5	1.0	0.4	—	1.4	0.4	1.0	0.5	0.8	1.5
30—34	4.7	2.7	4.4	1.0	0.7	1.0	1.0	1.1	2.0	2.6	0.9	1.5
35—39	1.6	4.1	2.6	0.3	0.7	0.5	0.3	1.9	1.3	1.1	1.4	0.8
40—44	3.9	4.6	2.9	0.6	1.3	0.9	1.4	1.3	0.6	2.0	2.0	1.5
45—49	6.3	7.4	8.7	2.0	1.8	2.3	1.4	1.3	2.6	2.8	4.2	3.9
50—54	11.0	11.2	11.0	1.3	3.7	3.4	1.3	1.4	1.7	8.4	6.0	5.9
55—59	9.3	15.9	18.4	3.0	6.2	5.2	1.3	1.0	3.7	5.1	8.7	9.4
60—64	17.5	23.7	30.2	2.6	7.2	9.5	2.6	2.5	6.3	12.4	14.0	14.4
65—69	17.1	25.1	39.7	4.1	2.8	14.4	2.1	4.5	8.4	11.0	17.8	16.8
70—74	19.6	39.4	57.0	5.2	10.1	15.4	2.1	8.4	7.2	12.4	20.9	34.4
75—79	22.3	31.1	49.0	7.4	9.9	13.0	—	1.4	7.2	14.8	19.8	28.8
80—84	—	30.4	68.2	—	18.2	34.1	—	3.0	3.1	—	9.1	31.0
85—	—	35.7	55.8	—	21.4	20.9	—	—	13.9	—	14.3	20.9
Age adjusted rate	5.6	7.5	9.7	1.1	1.8	2.5	1.5	1.9	2.8	3.1	3.8	4.4
Number of cases	274	413	486	51	102	127	73	99	139	150	212	220
						FEMALE						
0— 4	4.1	6.1	5.3	—	0.5	—	2.4	4.0	4.0	1.8	1.6	1.3
5— 9	2.7	3.2	4.0	—	—	0.5	1.1	0.9	2.1	1.6	2.3	1.3
10—14	2.6	2.0	2.3	0.5	—	0.3	0.9	0.7	1.3	1.2	1.2	0.7
15—19	1.7	1.6	1.6	0.4	0.2	—	0.9	0.7	1.0	0.4	0.7	0.6
20—24	1.3	1.0	1.9	0.4	—	—	0.2	0.2	1.6	0.6	0.8	0.3
25—29	2.3	1.8	1.4	0.2	0.2	0.2	0.9	0.8	0.5	1.2	0.8	0.7
30—34	2.0	2.4	2.1	0.3	0.2	0.5	0.8	0.6	0.2	1.0	1.5	1.4
35—39	2.9	1.9	2.3	1.3	0.5	0.5	0.5	0.9	1.0	1.0	0.5	0.8
40—44	3.1	4.2	4.8	0.6	0.7	1.4	0.6	1.7	2.0	1.9	1.7	1.4
45—49	4.7	4.2	7.3	1.5	1.1	0.3	1.5	0.5	2.2	1.8	2.6	4.8
50—54	10.0	9.2	13.1	3.4	2.4	2.7	0.7	2.1	2.3	5.8	4.7	8.0
55—59	11.0	10.7	20.1	2.2	2.9	6.0	1.3	1.1	3.4	7.5	6.8	10.4
60—64	13.3	12.4	22.3	2.0	5.4	4.9	3.9	1.2	4.0	7.4	5.8	13.9
65—69	6.2	16.8	24.8	0.6	5.6	6.1	0.6	1.0	4.4	5.0	10.2	14.3
70—74	28.1	22.6	32.6	8.2	6.6	8.5	5.4	8.0	4.7	14.5	8.0	19.4
75—79	21.7	18.2	34.8	7.7	4.6	7.9	1.5	3.4	4.5	12.4	10.2	22.5
80—84	8.8	6.6	31.6	2.9	—	15.8	2.9	2.2	—	2.9	4.4	15.8
85—	5.6	9.2	21.6	—	—	4.3	—	—	4.3	5.6	9.2	13.0
Age adjusted rate	5.0	5.2	7.5	1.1	1.1	1.5	1.2	1.4	2.1	2.7	2.6	3.9
Number of cases	245	294	403	55	67	86	59	77	105	131	150	212

Connecticut State Department of Health 1955. Table 4, pp. 32, 37, 38, and Appendix Table A pp. 123, 124, 133.

Table 9.
(Dorn & Cutler)
U. S. A. 1947. Incidence Rates per 100.000.

	Lymphogranulomatosis				*Leukæmia*				*Other Lymphoma*			
	White Males	White Females	Non-white Males	Non-white Females	White Males	White Females	Non-white Males	Non-white Females	White Males	White Females	Non-white Males	Non-white Females
Age												
0— 4	0.0	0.2	0.0	0.0	7.1	7.6	4.7	1.9	0.7	1.6	0.9	2.8
5— 9	0.7	0.2	0.0	0.0	4.3	3.1	1.1	1.2	1.3	0.9	2.4	0.0
10—14	1.7	1.3	4.0	0.0	4.2	3.3	2.7	0.0	2.2	0.7	0.0	0.0
15—19	2.5	0.9	1.5	1.3	2.7	1.2	1.5	0.0	1.2	1.0	1.5	2.7
20—24	2.3	4.4	0.0	2.1	3.3	1.3	2.7	2.1	0.8	0.9	5.3	0.0
25—29	2.8	2.6	4.4	1.9	1.5	2.4	3.3	0.9	2.4	1.4	3.3	3.7
30—34	3.3	3.7	3.7	0.0	4.5	2.0	4.8	1.0	4.5	2.0	1.2	0.0
35—39	3.3	2.7	2.3	2.1	3.7	4.0	9.3	0.0	4.7	2.5	4.7	5.2
40—44	3.7	2.7	2.6	1.3	4.6	3.4	4.0	3.9	6.7	4.9	1.3	5.1
45—49	5.8	2.8	1.5	1.5	7.9	6.5	13.1	6.0	9.1	4.7	11.7	10.6
50—54	5.5	3.6	5.5	4.0	10.6	11.6	9.1	0.0	12.8	10.3	21.8	10.1
55—59	6.1	4.2	8.0	5.9	19.3	13.6	10.7	11.8	24.9	12.7	8.1	2.9
60—64	7.3	4.1	0.0	4.2	19.1	18.0	23.6	12.5	16.5	18.7	43.2	20.9
65—69	9.9	3.8	9.8	0.0	32.3	20.5	29.5	17.6	29.2	20.1	14.8	13.2
70—74	8.4	3.5	0.0	0.0	40.5	17.7	47.8	0.0	28.7	20.6	19.1	42.1
75—79	6.0	4.5	18.0	0.0	58.7	15.7	36.1	0.0	34.7	24.7	0.0	0.0
80—84	6.6	2.2	0.0	31.4	46.6	22.4	83.7	0.0	30.0	11.2	0.0	0.0
85—	0.0	4.3	0.0	0.0	52.4	17.3	0.0	0.0	29.9	17.3	0.0	0.0
Age-adjusted rate	3.4	2.4	2.7	1.6	9.1	6.3	8.6	2.9	7.4	5.1	6.6	5.1
Number of cases	219	166	25	15	538	404	68	25	464	334	56	44

Morbidity from Cancer in the United States. Public Health Monograph No. 29. 1955. Table 4 a-d. pp. 87-90, and Table 6 a-d. pp. 92-95.

At this time appeared Dorn & Cutler's (1955) study on Morbidity from Cancer in the United States, based on information collected from ten metropolitan areas representing different geographical regions of the United States, namely: Atlanta, Birmingham, Dallas, and New Orleans in the south; San Francisco and Denver in the west; Chicago, Detroit, Philadelphia and Pittsburgh in the north. Except for New Orleans and Philadelphia, where the studies were confined to the city proper, the survey area included the central city and adjacent county or counties so that population statistics could be obtained from census populations. At the time of the first survey during 1937, 1938 or 1939 the population of the ten areas numbered about 13 million, or ten per cent of the total and 18 per cent of the urban population of the United States. At the time of the resurvey during 1947 and 1948, the estimated population was 14.6 million.

It follows from these principles that comparison with Danish material can best be carried out with the urban population of Copenhagen.

Figures from this valuable study are quoted in Table 9 and age distribution curve for incidence rates for Hodgkin's diseases is given in Fig. 10.

In the same year, 1955, Hewitt took advantage from the publication in England and Wales of mortality rates for leukæmia. Records for four years numbered 7,923 and showed the following geographical distribution:

Table 10 (Hewitt).
Leukaemia Mortality in the Standard Regions of England and Wales Standardized for Age and Sex, 1950—53.

Region	No. of deaths		Mortality ratio
	Actual	Standardized	
Southern	601	496.15	121
South Eastern ...	570	501.32	114
Greater London ..	1,685	1,483.29	114
Midland	768	763.84	101
Eastern	554	580.34	95
South Western ...	543	569.03	95
North Midlands ..	569	606.25	94
Yorkshire (East and West Ridings) .	683	735.93	93
North Western ...	1,069	1,162.01	92
Wales	421	471.12	89
Northern	460	553.69	83

In his analysis Hewitt finds a fairly regular gradient in leukæmia mortality from a relatively low level in the north of England to a level about half as high again in the south. That is, the variation is about as great as, (but in a generally *contrary* direction to) the regional variation in stillbirths and neonatal deaths, both of which are considered to be fairly sensitive to local conditions. The same general gradient can be observed in mortality ratios calculated for the sexes separately. Hewitt thinks that this north-to-south

gradient may owe something to the varying proportions of each economic class which are found in the different regions, but the regional differences in leukæmia — he says — are too large to be regarded as secondary to economic differences.

Table 11. (Hewitt).

Regions	Mortality Ratio	
	Aggregate of County Boroughs	Aggregate of Administrative Counties.
Difference	4.3	23.4
Five with high mortality ratios	100.7	107.8
Five with low mortality ratios	96.4	84.4

It appears that some of the great cities of England and Wales, apart from London, had an exceptionally high or low leukæmia death rate during 1950—52. Furthermore, the nine County Boroughs with teaching hospitals registered 618 deaths compared with a standard number of 606. Hewitt rightly considers this an evidence of similarity in diagnostic standard, but when he finds that regional variations can be shown to arise chiefly from variations in rates outside the main towns, it does not seem unlikely to us that difference in diagnostic standards outside the towns may play a part in the final result. According to the now rather common view, that good diagnostic facilities may not only mean the discovery of more cases, but also some causation of more cases, presumably in particular of leukæmia of myeloid type, it might be of interest if the English material from the various regions could be analysed with regard to per cent of myeloid and lymphoid cases. Due to the pronounced difference in age distribution of incidence rates between lymphoid and myeloid leukæmia a mere statement of the per cent of myeloid and lymphatic cases will not be sufficient for this purpose, because this per cent may change with the change in age distribution of the general population.

From the English Registrar-General's analysis of occupational mortality for the years 1930—32 (1938), for "leukæmia etc." which item includes Hodgkin's disease, Hewitt quotes the following Social Class mortality for males of all ages over 16:

Table 12. (Hewitt).

Social Class	Ratio
I Professional and administrative	176
II Intermediate	125
III Skilled manual workers	96
IV Intermediate	93
V Unskilled workers	84

Grouping together Social Classes "I and II" and "IV and V" gave the following ratios:

Age	I and II	IV and V
16—34	1.52	1
35—64	1.41	1
65 and over	2.05	1

The social grading for married women was as great as that for men.

Finding that employers and managers as a whole — all in Social Class II, had a mortality ratio as high as that of Social Class I, the author ascribes the social differences to some factor common to all well-paid persons at the time. He reports that an abbreviated analysis of mortality in the different economic strata of England and Wales has been prepared by the Registrar-General from the deaths registered during 1950 together with the ONE per cent sample of the 1951 census records, and that this indicates a social distribution of leukæmia which is:

I) unfavourable to the higher income groups
II) more uneven at ages over 65 than during working life.

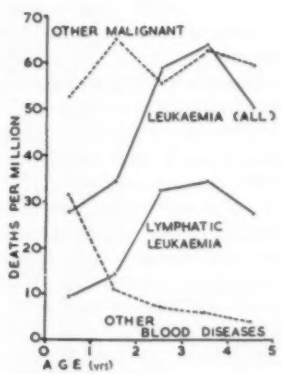


Fig. 7. (Hewitt).

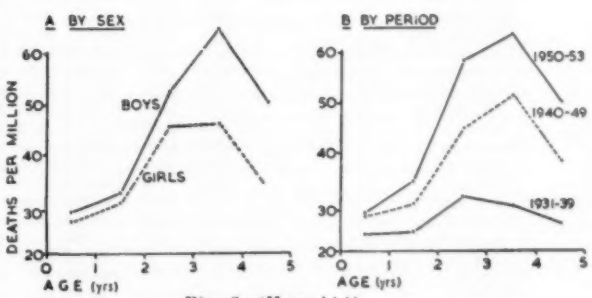


Fig. 8. (Hewitt).
Mortality from Leukaemia in Children under 5 Years of Age, 1931—53.

Furthermore, Hewitt's paper contains an interesting analysis of the peak of mortality from

Table 14. (Mac Mahon).
Leukemia Death Rates and Characteristics for the white Population of States and Divisions of the United States, 1949—53 and 1938—42.

Division and State	Number of leukemia deaths 1949–53			Standardized death rate per million, 1949–53			Corrected sex ratio 1949–53 (percent male)	Comparative mortality index 1949–53	Comparative mortality index 1938–42	Percentage increase from 1938–42 to 1949–53	Mean yearly increment in leukemia death rate [1]		Physicians per 100,000 population, 1949
	Male	Female	Total	Male	Female	Total					1938–45	1946–53	
New England	**1, 687**	**1, 331**	**3, 018**	**71. 8**	**52. 7**	**62. 2**	**57. 7**	**97**	**67**	**45**	**1. 8**	**2. 0**	**151**
Maine	136	108	244	56. 5	43. 5	50. 0	56. 5	78	55	42	1. 5	—. 2	97
New Hampshire	97	84	181	67. 2	54. 2	60. 7	55. 4	95	47	102	2. 6	1. 8	126
Vermont	80	69	149	80. 3	67. 4	73. 8	54. 4	114	57	100			140
Massachusetts	881	683	1. 564	75. 0	52. 6	63. 7	58. 8	99	73	36	1. 5	2. 6	170
Rhode Island	111	87	198	58. 9	42. 5	50. 7	58. 1	78	59	32	. 8	1. 6	118
Connecticut	382	300	682	77. 6	58. 2	67. 9	57. 1	105	69	52	2. 8	1. 5	152
Middle Atlantic	**5, 400**	**4, 171**	**9, 571**	**75. 9**	**56. 5**	**66. 2**	**57. 3**	**103**	**75**	**37**	**1. 4**	**2. 5**	**161**
New York	2, 908	2, 177	5, 085	82. 4	59. 0	70. 6	58. 3	110	83	33	1. 7	2. 4	196
New Jersey	862	645	1. 507	77. 0	55. 3	66. 1	58. 2	103	72	43	1. 6	2. 6	128
Pennsylvania	1, 630	1, 349	2, 979	66. 2	53. 5	59. 8	55. 3	93	65	43	2. 0	2. 5	128
East North Central	**5, 516**	**3, 875**	**9, 391**	**75. 1**	**53. 2**	**64. 1**	**58. 5**	**100**	**68**	**47**	**2. 0**	**2. 5**	**118**
Ohio	1, 473	1, 077	2. 550	76. 7	55. 4	66. 0	58. 1	103	63	63	1. 6	3. 8	116
Indiana	691	478	1, 169	71. 1	49. 2	60. 1	59. 1	93	58	60	2. 0	1. 2	103
Illinois	1, 551	1. 122	2. 673	74. 1	53. 4	63. 5	58. 1	99	76	30	1. 5	1. 7	141
Michigan	1, 096	708	1, 804	75. 0	50. 3	62. 6	59. 9	97	66	47	1. 4	2. 7	106
Wisconsin	705	490	1, 195	78. 2	56. 7	67. 4	58. 0	105	75	40	2. 5	3. 2	104
West North Central	**2, 948**	**2, 056**	**5, 004**	**79. 7**	**58. 1**	**68. 8**	**57. 8**	**107**	**71**	**51**	**2. 0**	**3. 5**	**113**
Minnesota	749	481	1, 230	94. 3	64. 2	79. 2	59. 5	124	90	38	—. 5	3. 7	132
Iowa	572	393	965	78. 6	55. 6	67. 1	58. 6	105	67	57	4. 0	3. 7	105
Missouri	711	510	1, 221	71. 4	50. 3	60. 8	58. 7	95	61	56	1. 9	2. 7	120
North Dakota	101	85	186	63. 7	63. 1	63. 4	50. 2	97	74	31	2. 7	1. 9	75
South Dakota	141	82	223	83. 5	55. 7	69. 5	60. 0	108	69	57	1. 6	2. 4	73
Nebraska	287	193	480	79. 6	55. 7	67. 6	58. 8	106	70	51	4. 0	3. 9	113
Kansas	387	312	699	77. 5	63. 7	70. 6	54. 9	110	67	64	1. 1	4. 9	103
South Atlantic	**2, 444**	**1, 804**	**4, 248**	**67. 6**	**50. 3**	**58. 9**	**57. 3**	**91**	**56**	**63**	**1. 9**	**2. 1**	**96**
Delaware	56	35	91	83. 2	49. 7	66. 4	62. 6	103	66	56			126
Maryland	290	238	528	64. 9	49. 7	57. 2	56. 6	89	62	44	1. 7	2. 1	136
District of Columbia	99	73	172	84. 0	52. 2	67. 9	61. 7	104	95	9	—. 3	—1. 3	267
Virginia	356	283	639	62. 0	48. 6	55. 2	56. 1	87	55	58	2. 6	1. 5	91
West Virginia	307	195	502	69. 3	46. 1	57. 6	60. 1	90	49	84	1. 9	2. 5	84
North Carolina	382	317	699	61. 0	49. 8	55. 4	55. 1	89	54	65	1. 9	1. 8	79
South Carolina	175	136	311	70. 1	49. 6	59. 8	58. 6	89	45	98	2. 1	1. 5	69
Georgia	373	268	641	72. 2	50. 4	61. 2	58. 9	95	58	64	1. 5	2. 2	84
Florida	406	259	665	71. 7	46. 1	58. 8	60. 9	92	51	80	1. 8	3. 9	91
East South Central	**1, 372**	**1, 003**	**2, 375**	**67. 9**	**49. 1**	**58. 4**	**58. 0**	**93**	**48**	**94**	**1. 7**	**2. 7**	**79**
Kentucky	418	307	725	63. 1	47. 4	55. 2	57. 1	86	43	100	2. 1	3. 0	84
Tennessee	425	343	768	68. 4	53. 0	60. 6	56. 3	102	52	96	1. 6	3. 0	90
Alabama	332	227	559	72. 0	47. 7	59. 7	60. 2	92	43	114	1. 9	2. 8	68
Mississippi	197	126	323	71. 6	45. 9	58. 7	60. 9	91	56	63	. 8	1. 3	64
West South Central	**2, 053**	**1, 434**	**3, 487**	**73. 5**	**51. 1**	**62. 2**	**59. 0**	**97**	**53**	**83**	**1. 7**	**3. 3**	**95**
Arkansas	240	161	401	65. 7	46. 4	56. 0	58. 6	87	40	118	2. 8	3. 7	82
Louisiana	316	209	525	81. 2	50. 6	65. 8	61. 6	102	55	85	1. 6	3. 3	104
Oklahoma	376	267	643	73. 6	53. 3	63. 4	58. 0	98	44	123	2. 4	4. 8	94
Texas	1. 121	797	1, 918	74. 3	52. 2	63. 2	58. 7	98	59	66	1. 0	2. 8	95
Mountain	**850**	**609**	**1, 459**	**72. 4**	**55. 8**	**64. 1**	**55. 9**	**100**	**56**	**79**	**. 9**	**3. 9**	**110**
Montana	130	85	215	81. 8	64. 6	73. 2	55. 9	113	67	69	1. 6	5. 5	94
Idaho	127	77	204	85. 7	59. 5	72. 5	59. 0	114	50	128	. 8	8. 1	77
Wyoming	36	27	63	51. 8	48. 7	50. 3	51. 5	75	53	42			83
Colorado	229	187	416	69. 3	57. 6	63. 4	54. 6	99	59	68	. 3	3. 4	158
New Mexico	79	60	139	56. 7	49. 1	52. 9	53. 6	85	46	85	1. 6	. 0	73
Arizona	102	78	180	69. 0	53. 1	61. 0	56. 5	96	51	88	—. 2	4. 7	97
Utah	117	77	194	80. 1	50. 7	65. 3	61. 2	102	55	85	2. 4	4. 5	115
Nevada	30	18	48	75. 0	57. 2	66. 1	56. 7	103	52	98			110
Pacific	**2, 802**	**2, 077**	**4, 879**	**80. 5**	**59. 3**	**69. 9**	**57. 6**	**107**	**75**	**43**	**2. 6**	**2. 3**	**132**
Washington	477	312	789	77. 3	54. 7	65. 9	58. 6	97	70	39	3. 4	2. 0	106
Oregon	337	195	532	84. 4	52. 7	68. 5	61. 6	107	71	51	3. 6	4. 3	109
California	1, 988	1. 570	3. 558	81. 0	61. 3	71. 0	56. 9	110	77	43	1. 6	2. 0	142

[1] Values are not Calculated for States with less than 500,000 white Population in 1950.

leukæmia among children aged under five, generally ascribed mainly to lymphatic leukæmia. For the period 1931—53 he finds that this phenomenon appears to affect boys more than girls, and to have become more important during recent years, and he reports a similar increase in death rates among babies in U. S. A. since 1931, between the second and third years of life, which seems to have been greater for the first post-war babies. This problem will be discussed on pages 99 and 103 and Hewitt's international comparison on page 95.

The difference between urban and rural populations with regard to leukæmia mortality rates was discussed by Meadors (1956) on the basis of United States figures from 1944—48. He found significantly higher death rates in urban populations at certain ages, while at other ages rates were similar for urban and rural populations. To Meadors this appears inconsistent with the hypothesis that the higher crude rates in urban population can be accounted for by superior diagnostic services in cities.

Table 13. (Meadors).

Average Annual Mortality Rates from all Forms of Leukemia per 1 Million white Population for Urban and Rural Residents, According to Age and Sex, United States, 1944—48.

Age in years	Male		Female	
	Urban	Rural	Urban	Rural
0–4	61. 56	50. 17	54. 81	40. 99
5–9	38. 30	25. 60	26. 84	19. 36
10–14	27. 43	15. 48	19. 93	14. 31
15–19	30. 61	21. 97	17. 10	12. 76
20–24	20. 29	21. 58	13. 96	12. 95
25–29	22. 50	17. 19	17. 26	12. 45
30–34	31. 26	20. 47	22. 65	15. 33
35–39	30. 20	20. 52	28. 06	18. 81
40–44	39. 43	29. 60	30. 28	23. 15
45–49	57. 28	37. 75	47. 05	32. 14
50–54	86. 00	59. 42	66. 17	42. 59
55–59	126. 32	89. 21	97. 85	63. 07
60–64	180. 08	115. 93	104. 74	86. 75
65–69	228. 45	144. 67	140. 30	102. 53
70–74	292. 71	200. 52	169. 89	127. 57
75 and over	318. 93	184. 13	174. 39	107. 14
Total	67. 35	45. 83	48. 39	32. 75

The present authors are inclined to find Meadors' figures in full accordance with the assumption that diagnostic services may in towns be more accessible to — or anyhow more used by — the elderly, than in the country — an assumption which may prove justified also outside the United States.

Prior to 1949 reports on deaths from leukæmia in the United States did not include a breakdown by age for deaths from this cause in the individual States, but with an interval of three months Walter & Gilliam (1956) and Mac Mahon (1957) published analyses of the geographical distribution in the United States of leukæmia mortality respectively for 1949—1951 and 1949—1953.

Walter & Gilliam in their tables give standardized mortality ratios for whites and nonwhites in each State for both sexes together, compared with death rates for the United States as a whole, according to age and race, and applied to the appropriate populations of individual states to determine the deaths expected in each, if no regional variation from this standard United States experience existed. They find mortality ratios for leukæmia tending to be greater in the Northern United States than in the Southern, and this applies to both males and females of white and nonwhite races. In states with a significantly higher-than-average death rate, excess death rates were found at all ages, but the excess increased with age. The peak in death rate among white children between 3 and 4 years of age was not observed in nonwhite death rates.

MacMahon confines his study to the white population giving standardized death rates for each sex in each state, comparing areas with respect to the increase in leukæmia death rate noted since the period 1938—42.

The author attempts an adjustment of death rates for various divisions of the United States with regard to the varying degree of urbanisation and based on the assumption derived from Meadors figures that the rates for the urban population are 1½ times higher than those for the rural population in each division.

This adjustment raises the rates for the southern division (cf. Table 14) relative to divisions in the northeast, and suggests that the originally low rates in the south may result from the lower percentage of urban population there. However, the adjustment has accentuated the difference between the west and the northeast. The three western divisions now rank first, second and third in order of leukæmia death rates.

Also in the evaluation of differences between states Mac Mahon calculates coefficients for the correlation of the comparative mortality index in each State with the percentage of the white population of the State classified as urban in 1950, the median income of the white population in 1949, and the number of active non-Federal physicians per 100,000 population in 1949.

The correlation with the percentage of urban population was small and insignificant ($r=0.13\pm 0.14$), but higher correlations were found with both median income ($r=0.27\pm0.14$) and density of physicians ($r=0.35\pm0.14$). Partial correlation suggested closer association of the leukæmia deathrate with density of physicians when income was kept constant ($r = 0.24$) than with income with physician density constant ($r = 0.06$).

MacMahon further studies whether the geographic patterns have undergone recent changes, realizing that it is not to be expected that the

Table 15. (Mac Mahon)

Age-specific Leukemia death Rates in Each Division, as a Percentage of the United States Rate for the Same Age Group, 1949—53.

Age	Pacific	West North Central	Middle Atlantic	East North Central	Mountain	New England	West South Central	South Atlantic	East South Central	Death rate per million, United States
0–4	114	101	95	106	97	99	102	89	89	58. 7
5–14	126	98	105	98	103	107	92	89	87	31. 7
15–24	106	101	109	99	89	101	89	88	110	20. 8
25–34	107	100	111	94	107	89	93	91	111	22. 5
35–44	100	103	112	98	102	85	96	89	101	33. 2
45–54	103	106	104	96	98	99	96	97	97	62. 3
55–64	102	105	107	99	97	97	98	89	89	129. 7
65–74	108	112	103	105	102	92	92	87	88	238. 7
75+	119	123	95	99	103	105	108	104	79	339. 1
Total	107	105	101	98	98	96	95	90	90	64. 4

geographical pattern should be explained in terms of any one variable or influence. He points to the effect of urbanization, higher income, better medical care, and more accurate diagnosis. In addition he points out that the possibility that some feature of medical care is itself leukæmogenic cannot be overlooked. Finally the possible effect of radioactivity deposited from atomic tests is discussed in view of the relatively rapid recent increase in leukæmia death rate for certain Mountain States, particularly Nevada, Utah, Arizona, Idaho, and Montana. However, the author points to the fact that after the initial atomic explosion in New Mexico in 1945, a relatively small one, no tests were conducted in the United States until 1951, but the upward trend in leukæmia death rates commenced about 1947—48. Furthermore, later studies show less correspondance of radioactive fallout to the pattern of leukæmia increases, and it is considered that the biological effects of fallout in the amounts observed are trivial. It should be remembered that while he was working on a material of death certificates a specification of cases into myeloid and lymphoid types has been out of reach to the author.

Coincident in time with the two last mentioned papers, articles appeared by Mac Mahon & Clark (1956), and Mac Mahon & Koller (1957) on leukæmia studies among the 2,700,000 population of the Borough of Brooklyn, during the ten-year period 1943—1952. Reports were collected on residents diagnosed for the first time during this period as having leukæmia and 33 hospitals representing 95 per cent of the hospital beds assigned to general or chronic diseases showed 1481 records of inpatients, while it was found practically impossible to assemble records of domiciliary and outpatient treatment.

The addition of 311 abstracts from records of hospitals outside Brooklyn gave a total of 1792 hospital abstracts referring to 1490 patients, while a study of death certificates added 400 cases of which 219 were included in the material. Out of the total of 1709 patients 40 men and 31 women were negroes and for two patients colour was

Table 16.

(Mac Mahon & Clark).

Incidence of Acute Leukemia Per Million Per Annum Related to Sex and Age at Diagnosis.

Age	Myelogenous			Lymphatic			Monocytic			Unknown			All Acute		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
0–9	18.2	22.6	20.4	14.1	13.2	13.7	2.0	1.6	1.8	10.6	6.3	8.5	44.9	43.7	44.3
10–19	13.4	11.7	12.5	9.3	2.3	5.8	1.7	0.6	1.2	4.1	3.5	3.8	28.5	18.1	23.3
20–29	6.9	8.2	7.6	2.5	1.8	2.1	0.0	1.4	0.7	1.0	1.8	1.4	10.4	13.3	11.9
30–39	10.5	15.9	13.3	2.0	1.4	1.7	2.0	1.8	1.9	0.5	1.8	1.2	15.1	20.8	18.1
40–49	16.7	16.2	16.5	1.6	1.0	1.3	1.6	4.7	3.2	1 1	1.6	1.3	21.1	23.6	22.3
50–59	19.2	27.4	23.2	3.3	10.0	6.6	3.3	3.3	3.3	6.6	4.7	5.6	32.4	45.4	38.9
60–69	25.2	36.7	31.1	9.5	2.0	5.7	5.3	7.1	6.2	8.4	6.1	7.3	48.4	52.0	50.2
70+	24.5	25.8	25.2	13.4	7.4	10.1	6.7	3.7	5.0	6.7	12.9	10.1	51.3	49.8	50.5
Total	15.2	18.4	16.8	6.1	4.6	5.3	2.2	2.6	2.4	4.3	3.8	4.1	27.7	29.4	28.6

Table 17.
(Mac Mahon & Clark).
Incidence of Chronic Leukemias Per Million Per Annum Related to Sex and Age at Diganosis.

Age	Chronic Myeloid			Chronic Lymphatic			All Other (Except Acute)			All Leukemias (Including Acute)		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
0–9	1.5	0.5	1.0	0.0	0.5	0.3	4.0	3.2	3.6	50.4	47.9	49.2
10–19	2.3	2.3	2.3	0.0	0.0	0.0	0.6	1.8	1.2	31.4	22.2	26.8
20–29	6.9	3.7	5.2	0.5	0.5	0.5	0.0	0.9	0.5	17.8	18.3	18.1
30–39	11.6	7.7	9.5	4.0	3.2	3.6	4.5	0.9	2.6	35.2	32.6	33.8
40–49	17.3	14.7	16.0	10.3	6.8	8.5	6.5	5.8	6.1	55.1	50.8	52.9
50–59	28.4	25.4	26.9	40.3	18.7	29.6	15.2	11.3	13.3	116.4	100.8	108.6
60–69	37.9	32.6	35.2	101.0	52.0	76.1	33.7	26.5	30.0	221.0	163.2	191.6
70 +	53.5	27.6	39.4	167.3	70.0	114.0	44.6	31.3	37.3	316.7	178.8	241.1
Total.....	14.4	11.1	12.7	20.8	10.8	15.7	8.4	6.5	7.4	71.3	57.7	64 4

unknown. By standardization for age the ratio of incidence in whites to incidence in negroes was reduced from 1,7: 1 to 1.3: 1, and for further study only the data for 1636 white patients were used.

Like Clemmesen, Busk & Nielsen (1952), Mac Mahon & Clark find that each pathological variety of leukæmia has its own distinct age incidence curve. Their incidence rates by age will be illustrated in diagrams for comparison with corresponding Danish figures later in this paper, and the basic figures are quoted as Tables 16 and 17.

Mac Mahon & Koller (1957) now compared the 1636 Brooklyn patients with selected census data for the population. They found that persons born in Russia constituted a larger part of the leukæmia group (39.6 per cent) than of the general population (26.2 per cent) (difference 13.4±1.7), and since practically all of the Russian-born population of Brooklyn are of Jewish ancestry it was examined by means of the cemetery of burial whether leukæmia was more frequently stated as cause of death among Jews than among others. A series of 1368 deaths from leukæmia was compared with a systematic one in 200 samples of all deaths in the same area, and it appeared that leukæmia was recorded twice as frequently among Jews, as among others. This relationship was seen in both native-born and foreign-born groups, in males and females, at all ages and in all the common varieties of leukæmia. Groups predominantly Catholic or Protestant showed no difference.

Mac Mahon & Koller point out that the Brooklyn income differential between whites and negroes is lower than in many parts of the United States. Also facilities for medical care are extensive and widely available to all. For instance, in 1949 there were 159 active physicians per 100,000 population compared with the national average of 135. On this background the authors point to the local similarity in White and Negro leukæmia rates and find, that Negro populations comprise more young persons, more women and more rural dwellers than the white, all of which will tend to give low national leukæmia rates for Negroes.

On the basis of data, quoted in our Table 19 the authors find the association between the ratio of the median incomes obvious on inspection. The correlation between the two variables is 0.72 ± 0.22. Mac Mahon & Koller therefore find is most likely that the higher national leukæmia death rate in whites compared with Negroes is attributable to a higher recorded rate among persons in that social complex which is closely measured by income, and which includes urbanization, higher income, better medical care, and more complete diagnosis.

Table 18.
(Mac Mahon)
Percentage Distribution According to Religions Affiliation of Cemetery of Burial and Type of Leukæmia.

Diagnosis	Percentage distribution				Number of patients
	Catholic	Jewish	Protestant	Total	
Comparison sample	42.2	32.8	25.0	100.0	1038
Acute myelogenous leukemia	26.3	57.2	16.5	100.0	350
Chronic myelogenous leukemia	33.3	48.4	18.3	100.0	244
Chronic lymphatic leukemia	27.1	53.9	19.0	100.0	295

In each diagnosis, the leukemia series is standardized to the age distribution of the comparison sample.

Table 19.
(Mac Mahon & Koller)
Mean Annual Leukemia Death Rates in Whites and Non-Whites in 22 States, 1949—1953.

State	Age and sex standardized leukemia death rate		Median income in 1950 ($)		Ratio: white divided by non-white	
	White	Non-white	White	Non-white	Leukemia	Income
Alabama	5.92	2.91	1455	616	2.03	2.36
Arkansas	5.52	2.38	1117	488	2.32	2.29
Florida	5.82	2.71	1737	847	2.15	2.05
Georgia	6.04	2.44	1515	610	2.48	2.48
Illinois	6.30	4.34	2393	1811	1.45	1.32
Indiana	5.93	3.93	2140	1625	1.51	1.32
Kentucky	5.46	3.33	1411	862	1.64	1.64
Louisiana	6.49	4.62	1767	774	1.40	2.28
Maryland	5.65	4.41	2261	1184	1.28	1.91
Michigan	6.19	5.50	2441	2175	1.13	1.12
Mississippi	5.79	3.03	1236	439	1.91	2.82
Missouri	6.29	3.84	1741	1154	1.64	1.51
New Jersey	6.53	4.60	2464	1531	1.42	1.61
New York	6.98	4.67	2401	1693	1.49	1.42
North Carolina	5.46	3.85	1567	712	1.42	2.20
Ohio	6.52	4.69	2252	1607	1.39	1.40
Pennsylvania	5.91	5.26	2162	1527	1.12	1.42
South Carolina	5.90	2.74	1684	525	2.15	3.21
Tennessee	5.97	3.73	1374	799	1.60	1.72
Texas	6.24	3.46	1754	817	1.80	2.15
Virginia	5.46	3.29	1880	919	1.66	2.05
West Virginia	5.68	4.50	1859	1531	1.26	1.21

In support of this conclusion the authors further point to the earlier result of Mac Mahon, previously reviewed, that rates for the individual states were more closely associated with the number of physicians per 100,000 population in the same states than with measures either of urbanization or of income. They conclude that it may well be that access to or use of medical care is the variable most directly concerned in this association, and add that a recent study of a sample of households in New York City showed the percentage of persons who had received physician care in the previous year was appreciably higher for the Jewish than for the Protestant or Catholic groups. However, it is found unlikely that the whole of the Jewish/non-Jewish difference can be explained by differences in cases diagnosed, and it is suggested that there are "aspects of medical care which are themselves leukæmogenic"

Table 20. (Mac Mahon)
Mean Annual Incidence of Hodgkin's Disease in the White Population of Brooklyn, 1943 to 1952, According to Sex and Age of Patients.

Age at diagnosis	Number patients			Incidence per million		
	M	F	Total	M	F	Total
0— 4	0	0	0	0.0	0.0	0.0
5— 9	2	1	3	2.2	1.1	1.7
10—14	3	5	8	3.5	6.2	4.8
15—19	16	18	34	18.3	20.0	19.2
20—24	29	16	45	29.4	15.1	22.0
25—29	27	33	60	26.1	29.3	27.8
30—34	24	24	48	24.3	21.9	23.0
35—39	23	19	42	22.9	17.1	19.9
40—44	26	19	45	26.8	18.7	22.7
45—49	20	12	32	22.7	13.4	18.0
50—54	25	17	42	30.2	20.5	25.3
55—59	37	10	47	54.1	15.0	34.8
60—64	30	17	47	54.7	31.2	43.0
65—69	28	16	44	69.7	36.8	52.6
70—74	20	10	30	82.3	36.1	57.7
75 and more	11	8	19	53.6	30.1	40.3
All Ages	321	225	546	25.7	17.4	21.5

It may here be recalled that Panton & Valentine (1929) among 172 leukæmia cases from London Hospital from 1912—27, among the cases of known nationality found a ratio of Hebrews 1:1.4, while the ratio in the hospital in general was roughly estimated at 1:10. They suggested that the Hebrew race is particularly susceptible to this disorder.

Mac Mahon's incidence rates for Hodgkin's disease (1957) — Table 20 — will be the subject of further discussion in the international comparison later in this paper, where further information will be found. For Brooklyn he gives the annual incidence rates as quoted above. Following the method employed in the study already reviewed the religious affiliation of the cemetery of burial as indicated on the death certificate was used as index of religion, and thus Mac Mahon examined the percentage distribution by religion of a series of 367 deaths from Hodgkin's

disease and 1,119 comparison deaths. Respectively six and twenty-three cases in which patients were buried outside the city, and zero and fifty deaths under 1 years of age were excluded.

Table 21.
(Mac Mahon)

Percentage Distribution, by Religion, of Deaths from Hodgkin's Disease and a Comparison Sample of all Deaths, Brooklyn, 1943 to 1952.

Age at death*	Pt. group	No. pt.	Religion, % Catholic	Jewish	Protestant	Total
0-39	Hodgkin's disease	115	43.5	35.7	20.8	100
	Comparison sample	68	49.4	31.9	18.7	100
40 and more	Hodgkin's disease	246	34.2	45.9	19.9	100
	Comparison sample	978	42.9	32.2	24.9	100
ALL AGES	Hodgkin's disease	361	37.1	42.7	20.2	100
	Comparison sample	1,046	45.0	32.1	22.9	100

*In each age group, figures for the comparison sample are standardized to the age distribution of the Hodgkin's disease patients within the same group

From Table 21 Mac Mahon concludes that the ratio of proportions of deaths of Jewish patients in the Hodgkin's disease and comparison series suggests that after standardization for age differences Hodgkin's disease appears as cause of death about one and a half times more frequently among Jewish than among non-Jewish patients. A comparison separately for the age groups 0—39 and 40 and more showed the excess proportion of deaths among Jews in the Hodgkin's disease series to be almost entirely restricted to the later age period. The difference approaches significance ($10.2 \pm 5{,}6$) although the proportion of deaths among Jews in the comparison sample was about the same for the two age periods. It is therefore suggested by the author that Hodgkin's disease shares with leukæmia and lymphosarcoma the feature of more frequent diagnosis among Jewish than among non-Jewish people in Brooklyn.

IONIZING RADIATION

Since the demonstration by Krebs, Rask-Nielsen & Wagner in 1930 of an increased occurrence of leukæmia among mice subjected to Roentgen irradiation, the causative effect of ionizing radiation in leukæmia has been studied with increasing intensity.

Engelbreth-Holm (1941) among 15 cases of myelogenous leukæmia found two cases of carcinoma of the uterine cervix, and among 31 cases of lymphogenous leukæmia and 35 cases of lymphosarcoma nine cases of carcinoma, and suggested that either the incidence of leukæmia among old people is much higher than believed, or that there is a connection — "the nature of which, however is obscure" between the two diseases. Naturally, many of these cases were treated with irradiation before the development of the leukæmia, but the question how far irradiation has been causative is difficult to judge from the paper, because the sequence of the two affections is not clear.

March (1944, 1950) studied the occurrence of leukæmia among American radiologists for periods of 15 and 20 years, respectively, from 1929 to 1948 inclusive. He found that 65,922 non-radiological physicians died, of whom 334 died from leukæmia, while among 229 radiologists 14 died with leukæmia, making an overall incidence for the former category of 0.51 per cent and for the latter 4.68 per cent.

Henshaw & Hawkins (1944) compared the incidence of leukæmia among physicians and in the general population of the United States for the period 1939—1940, specified on leukæmia type for each year 1933—42 and distributed on five year age groups. Comparisons were made on the basis of (1) the ratio of deaths from leukæmia to deaths from cancer, (2) ratio of deaths from leukæmia to total death rates, and (3) death rates

Table 22.
(Dublin & Spiegelman 1947).

Annual Death Rates from the Principal Causes for Male Physicians Compared with White Males in the General Population, Ages 25 and Over; United States, 1938—1942.*

Cause of Death	Death Rates per 100.000: Male Physicians	Death Rates per 100.000: United States White Males	Ratio of Death Rates: Physicians to White Males
All causes of death.....	2,052.6	2,022.1	1.02
Leukemia and aleukemias	11.4	6.5	1.75
Biliary calculi and other diseases of the gallbladder	12.2	8.4	1.45
Intracranial lesions of vascular origin	222.8	185.9	1.20
Diseases of the heart and coronary arteries † ..	845.3	713.7	1.18
Arteriosclerosis	50.1	43.2	1.16
Cirrhosis of the liver	25.8	23.3	1.11
Pneumonia and influenza	112.5	103.0	1.09
Diabetes mellitus	44.5	41.2	1.08
Suicide	39.0	37.6	1.04
Automobile accidents ...	44.2	49.5	0.89
Cancer	198.4	244.5	0.81
Appendicitis	10.3	13.4	0.77
Hernia and intestinal obstruction	12.1	16.1	0.75
Nephritis †	119.3	162.9	0.73
Ulcer of the stomach or duodenum	12.8	20.8	0.62
Accidents other than automobile	50.6	84.0	0.60
Diseases of the prostate..	15.8	29.1	0.54
Tuberculosis	31.9	70.4	0.45
Syphilis	9.1	26.5	0.34

*) The general population death rates have been adjusted on the basis of the age distribution of male physicians in 1940.

†) The death rates relate to the period 1939—1942. Because of changes in the classification procedure (International List of Causes of Death) introduced in 1939, data for the general population for this cause are not comparable with those of earlier years.

Table 23.
(Dublin & Spiegelmann 1948)
Mortality Ratios According to Cause of Death. Ratio of Actual Deaths Among Medical Specialists at Ages 35 to 74 Years to the Deaths Expected on the Basis of Age-Specific Death Rates for All Male Physicians 1938—1943, Each Cause of Death Treated Separately.

	All Causes.	Cardio-vascular enal disease.	Diseases of Coron. art. and angina pect.	Cancer	Pneumonia and Influenza	Accidents	All Other Causes.
All Specialists	0.78*	0.81*	0.97	0.96	0.65*	0.70*	0.67*
Roentgenology and Radiology.	0.90	0.89	1.10	1.33	+	+	0.84

\+ less than five actual deaths were recorded in this category.
* significant in the statistical sense, that is the probability is less than 5 in 100 that the deviation of actual deaths from the expected deaths is at least as great as that observed in a chance occurrence.

from leukæmia, and it was found that leukæmia was recognized approximately 1.7 times more frequently among physicians, than among white males in the general population. After discussion of possible discrepancies the authors point out that while the data furnish no direct proof that radiation acts to incite leukæmia in human beings they are in accord with this possibility.

Ulrich (1946) presented a statistical study of 34,626 obituary notices in the Journal of the American Medical Association covering the ten-year period from 1935 to 1944 and found that the incidence of leukæmia among 205 physicians listed as radiologists was 3.9 per cent which is more than eight times as great as the incidence — 0.44 per cent — among those not listed as radiologists. Ulrich regards this marked difference as substantial evidence that exposure to radiation is a potential cause of leukæmia and reports a case of lymphatic leukæmia in a dermatologist who failed to take effective precautions.

Dublin & Spiegelman based their first study (1947) on the records of active and retired living physicians and on their deaths during the five year period 1938 to 1942, on file with the American Medical Association. At the middate of this period there was 175,159 living physicians in the country, and it appeared that the mortality from leukæmia among male physicians was one and three-fourths times that of white males generally. Although better diagnosis may account for some of this excess, the authors referred to the possibility that in some instances physicians might have acquired the disease as a result of exposure to X-rays.

The authors followed this theory up with a second study (1948) based on a tabulation of full time medical specialists listed in the American Medical Directory of 1940, and the deaths among corresponding specialists within the period previously examined. They found that the high mortality from cancer among roentgenologists and radiologists might be of special significance when viewed in conjunction with their mortality from leukæmia, which showed a higher number of deaths and a higher proportion of deaths from this cause than any other specialty. The five deaths due to leukæmia recorded for roentgenologists and radiologists is several times the number expected on the basis of the mortality experience of all male physicians, the standard of comparison. Although roentgenologists and radiologists constituted only 4.3 per cent of the living specialists, they had one quarter of the deaths from leukæmia among all specialists. The authors find the facts indicative of an extra hazard to roentgenologists and radiologists that may arise from their exposure to dangerous radiation.

Table 24.
(Peller & Pick, 1955).
Percentage of Leukemia and other Cancers to all Deaths).*

Age	In U.S. Physicians 1947—53			In U.S. White Males 1948—50		
	Leukemia	All other cancers	All cancers	Leukemia	All other cancers	All cancers
25—29	5.8	9.1	14.9	1.4	6.4	7.85
30—34	4.5	9.1	13.6	1.2	8.2	9.3
35—39	2.55	8.7	11.3	1.0	9.2	10.2
40—44	2.1	8.7	10.8	0.79	10.7	11.5
45—54	0.9	12.6	13.4	0.68	14.2	14.9
55—64	1.1	12.6	13.7	0.61	16.9	17.5
65—74	1.2	14.3	15.5	0.55	15.9	16.5
75—84	0.73	13.1	13.8	0.36	12.8	13.2
85+	0.5	8.4	8.9	0.15	7.7	7.9
All	1.09	12.8	13.9	0.54	14.1	14.64
At age distribution of all White Males	1.20	12.5	13.7	0.54	14.1	14.64

*) With given cause of death.

Peller & Pick (1952, 1955) compared cancer and leukæmia deaths among American physicians during the period 1947—53 with corresponding figures for white males for 1948—50. Out of 20,831 deaths the cause was known in 16,585 cases.

It was concluded that physicians of all age groups show excessive ratios of leukæmia, both in relation to general mortality and to mortality from cancer. For radiologists ratios are six times higher than for physicians in general. The authors pointed out that the latency period of this professional leukæmia is short, and urged protective measures against radiation.

Already before the last of these papers Lange, Moloney & Yamawaki (1954) published their report on Leukæmia in Atomic Bomb Survivors in Japan from 1948 to 1952 inclusive*).

Table 25.
Cases of Leukemia by Age (From Lange et al. 1954).

Date of birth	Hiroshima City and prefecture		Nagasaki City and prefecture	
	Pop.	Cases leuk.	Pop.	Cases leuk.
Men:				
1941—1945	6,667	2	6,157	2
1936—1940	5,210	2	6,209	2
1926—1935	14,041	5	13,648	3
1916—1925	5,679	5	4,167	3
1896—1915	16,261	6	12,322	4
1895 & before	9,308	3	7,576	1
Total	57,166	23	50,079	15
Women:				
1941—1945	6,579	5	6,213	2
1936—1940	5,139	2	6,153	1
1926—1935	14,160	6	14,339	4
1916—1925	11,941	7	10,290	1
1896—1915	20,011	6	15,507	
1895 & before	10,045	3	8,554	
Total	67,875	29	61,056	8

*) An earlier report on the period 1948—1950 was published by Folley, Borges & Yamawaki, 1952.

The data quoted in the table 25 have in the original paper been specified for various zones of distance from the hypocenter of radiation. It is pointed out that the number of cases presented are in reality minimum figures.

Lange et al. report that most young infants had been evacuated prior to the bombings, and that the number of leukæmia cases is almost identical for men and women among "exposed" individuals, *i. e.* persons present in the cities of Hiroshima and Nagasaki during the atomic bombings, while "nonexposed" show a male preponderance, presumably due to occupational exposure. Consequently, it is stressed that the nonexposed individuals cannot serve as proper controls for the exposed groups in any discussion of comparative incidence or type of leukæmia.

The three authors find that the leukæmogenic dose of irradiation is high and that the incidence of leukæmia is directly related to the amount of irradiation received. Among atomic bomb survivors, chronic myelogenous leukæmia was represented with 41 per cent of the cases, followed by acute myelogenous leukæmia with 26 per cent. Up to the time of publication only one case of chronic lymphatic leukæmia had been seen among the seventy-five exposed cases. It was noted that chronic lymphatic leukæmia was also infrequent in the nonexposed series, and an inquiry among Japanese hæmatologists supported the suspicion that chronic lymphatic leukæmia is comparatively rare in Japan.

It might be suspected that this phenomenon is ascribable to the relative rarity of old people in Japan, in comparison, for instance, with Denmark. However, this cannot explain the difference in incidence of lymphatic leukæmia to its full extent. We have computed the expected incidence rate for lymphatic leukæmia in the age groups between 15 and 69 years for the population of Hiroshima as given, under the assumption that the latter city showed the same age-specific morbidity rate as Copenhagen. By this procedure we arrive

Table 26. (Moloney & Kastenbaum).
Incidence of Leukemia in the Hiroshima Survivors Felated to Distance from the Hypocenter and the Presence of Severe Radiation Complaints.

Distance from hypo-center	Population*			Cases of leukæmia			Incidence		
	SRC†	NRC**	Total	SRC	NRC	Total	SRC	NRC	Total
0— 999	750	450	1,200	14	1	15	1: 53	1: 450	1: 80
1,000—1,499	2,250	8,250	10,500	15	9	24	1:150	1: 917	1: 438
1,500—1,999	1,750	16,950	18,700	3	2	5	1:583	1: 8,475	1: 3,740
2,000—2,499	950	16,250	17,200	1	1	2	1:950	1:16,250	1: 8,600
2,500 and over	850	49,650	50,500	0	4	4		1:12,412	1:12,625
Total	6,550	91,550	98,100	33	17	50	1:198	1: 5,385	1: 1,962

*) Population estimated and rounded off to the nearest 50 persons. These populations figures were based on the Commission's 1949 radiation census and the Japanese national census (1950). Numbers of survivors with severe radiation complaints were estimated from observations made by the Commission's department on 19,675 Hiroshima survivors of childbearing age (3).

†) SRC: severe radiation complaints (heavily irradiated).

**) NRC: no radiation complaints (lightly irradiated).

at an incidence rate for lymphatic leukæmia in Hiroshima of 21.6 per million for men and 12.7 for women against respectively 34.0 and 21.7 in Copenhagen.

Moloney & Kastenbaum (1955) bring the table cited as 26 illustrating the leukæmogenic effects of ionizing radiation on Atomic bomb survivors in Hiroshima City, related to distance from the hypocenter and the presence of severe radiation complaints.

Simpson, Hempelmann and Fuller, (1955) examined the subsequent history of 1400 of 1722 children who had received x-ray therapy to the thymus gland between 1925 and 1951. In 17 of these children malignant neoplasia is known to have developed including seven cases of leukæmia and six of carcinoma of the thyroid. This is a significantly higher incidence than was found among the untreated siblings of the irradiated children or in the general population. In addition nine treated children were found to have thyroid adenoma.

The three authors conclude that a relationship has been demonstrated between both the total malignant tumours and the thyroid neoplasia incidence and the type of treatment given, but no such relationship could be demonstrated in the case of leukæmia. The possible significance of these facts was discussed.

Alice Stewart, Webb, Giles & Hewitt (1956) inspired by Hewitt's results began an inquiry of parents to leukæmia children after the death of the child. The survey was restricted to children aged under five years, and attention was focussed on antenatal X-ray histories because of the growing peak for the second and third years of life appearing on the mortality curve for the latest years.

Originally children with other neoplasia diseases were used for control until it was discovered that they, too, showed an age distribution different from other causes of death, whereafter the authors used live controls matched for age and sex.

According to a preliminary record of results by Stewart (1957), by November, 1956, 1072 case-control pairs had been interviewed, and it had appeared that a history of antenatal abdominal X-ray was obtained nearly twice as frequently from the mothers of children who had died from leukæmia or cancer as from the mothers of live controls. Among the 515 cases of leukæmia, 15 children were mongolian idiots.

The difference between cases and controls in respect to radiation was not due to difference in birth, rank or social class, nor to differences in maternal age. Stewart is inclined to believe that total body exposure to ionizing radiation shortly before birth causes a significant increase in the risk of developing cancer or leukæmia in childhood but wants to await a more detailed examination of records before she regards this as certain. It is noted that the association between leukæmia and mongolic idiocy appeared to be independant of any histories of irradiation.

Table 27. (Stewart).
Malignant Disease in Childhood and Diagnostic Irradiation in Utero.

Group	Number of children	Children irradiated in utero	
		Number	Per cent
Controls	1,072	79	7.4
Cases of:			
Leukæmia	515	63	12.2
C.N.S.	168	20	11.9
Renal	103	16	15.5
Neuroblastomas ..	91	18	19.8
Lymph nodes	70	6	8.6
All other sites	125	20	16.0
All cases of malignant disease	1,072	143	13.3

It may not be superfluous here to point to the possibility that a diagnosis of leukæmia may be arrived at more easily than average in a child benefitting from modern hospital facilities including abdominal X-ray of the mother before birth, but it would seem that until further information is obtained such radiological pelviometry should not be administered without medical indication of its necessity in the single case. Court-Brown & Doll (1957) in a monograph published by the British Medical Research Council have in great detail analyzed case records of 13,352 patients who had received X-ray treatment for ankylosing spondylitis at 81 British radiotherapy centres during the period 1935—1954 inclusive.

Table 28. (Court-Brown & Doll).
The Observed and Expected Numbers of Deaths Certified as Due to Leukaemia and Aplastic Anaemia, 1935—54: Study Series.

Disease group	Sex	No. of deaths		
		Minimum expected	Maximum expected	Observed
Leukaemia (International list Code no. 204)	M.	1.25	2.06	22
	F.	0.19	0.34	0
	M. and F.	1.44	2.40	22
Aplastic anaemia (International list Code no. 292-4)	M.	0.12	0.20	10
	F.	0.03	0.05	1
	M. and F.	0.15	0.25	11

Significance of difference between observed and maximum expected number of deaths:—
Leukaemia: $P < 0.000001$
Aplastic anaemia: $P < 0.000001$

Table b.
The Types of Leukæmia were Represented as Seen in the Second Half of the Table.

Type	No. of deaths certified	No. of deaths expected	p
Lymphatic	4	0.86	0.01
Myeloid	9	1.49	0.00003
Monocytic	4	0.34	0.0005
Other and unspecified	11	0.21	0.000001

Thus, all types of leukæmia show an excess, but this is least marked for lymphatic leukæmia.

A diagnosis of leukæmia, aplastic or hypoplastic anæmia or myelofibrosis was recorded on the death certificate of 46 of the patients who had died by December 31, 1955, while three patients still alive on this date were found to have leukæmia. In 28 of these cases death was ascribed to leukæmia, while in 12 it was certified as attributable to aplastic anæmia.

From national statistics the number of expected deaths was now calculated on the assumption that all persons untraced in 1955 were, in fact, alive and domiciled in Britain at the end of that year. It amounted to 2.9 for leukæmia and 0.3 for aplastic anæmia, so that the excess of mortality for both diseases found in the material under investigation is highly significant.

Court-Brown & Doll on the basis of ten cases available estimate the latent period at two to five years, but it should be noticed that this does not necessarily apply to for instance lymphatic leukæmia, sparsely represented as this type is. It should be mentioned that the authors discuss the possible leukæmogenic effect of drugs like gold and amidopyrine, but arrive at the conclusion that if it were assumed that drugs were largely responsible for the development of leukæmia, the frequency of their use should have been directly related to radiation dose, as they found the frequency of leukæmia to be. Nevertheless, it is emphasized by the authors that a number of approximations have been necessary to arrive at the quantitative estimation of the relationship between the dose of radiation and the incidence of leukæmia, so that this estimate may be subject to appreciable error.

The problems around leukæmia and the dosage of ionizing radiation were only touched upon by Court-Brown & Doll who find it a reasonable deduction, although not the only hypothesis compatible with their data, that there is no threshold dose. This and other dosage questions are treated by Lewis (1957) in a review of available evidence, of which most has been reviewed in the present paper from the viewpoint of incidence. It may perhaps be pointed out that Lewis's evaluation of leukæmia incidence is based only on the Brooklyn material collected by MacMahon, and that Busk's (1952) amplification of Videbæk's monograph is not considered in the assessment of the possibility of genetic factors in leukæmia. The material on hand is given under the following categories: 1) Leukæmia in Hiroshima and Nagasaki, 2) Leukæmia and Ankylosing Spondylitis, 3) Leukæmia and Thymic Enlargement, and 4) Leukæmia among Radiologists.

To the present authors it would seem premature to join Lewis in the conclusion from the paper by Lange et al. "that radiation induces the same pathological types that are found spontaneously and, as far as can be judged by the limited data, induces them in roughly the same relative proportions that occur spontaneously. This is especially evident in the case of chronic lymphocytic leukæmia, which is rare in both the exposed and unexposed Japanese populations, whereas it is the most common form of leukæmia after age 50 in the United States". As demonstrated elsewhere in the present paper (pp 98 and 99) the rates available from Japan point to special circumstances in that country. The difference in age distribution between myeloid and lymphatic leukæmia seems in itself to demand that all computations on incidence if possible should distinguish between the two categories. After all, the higher average age for lymphatic leukæmia cases might perhaps mean that the latency period for this neoplastic disease is longer than for myeloid leukæmia, and in the material of Court-Brown & Doll there were three lymphatic cases, which may have been caused by irradiation.

The student of incidence of malignant diseases in general might perhaps wonder if the precision of measurement of ionizing radiation under experimental conditions will allow sufficient accuracy to estimate under field conditions the dosage of radiation from atomic bombs and roentgen tubes necessary to provoke leukæmia, on the basis of 75 cases from Japan, 28 cases of Court-Brown & Doll, 7 cases of Simpson et al., and 17 cases among American radiologists, — in particular when the probable influence of fractionation of dose is considered. To this comes the possible additional leukæmogenic effects of other agents like myelotoxic drugs as gold or amidopyrine which might well be of significance to the—rare—development of leukæmia. If we consider the long latent period for other malignant diseases, including the lung cancer caused through radioactivity, it may not be unlikely that the incidence and the short latency period observed up to now, will represent just the feeble forebodings of a far more massive development, so that the cases seen up to now are just the first, and disposed individuals. To this comes the fact that the casualties caused by the atomic bomb directly will dominate the picture.

The answer to this is, that Lewis has not claimed more than an estimate of the order of magnitude of leukæmogenic dose of ionizing radiation which he gives as a range from 0.7×10^{-6} to 6×10^{-6} per rad per year. In the present connection it is particularly interesting that Lewis estimates that 10 to 20 per cent of the spontaneous incidence in Brooklyn may result from natural radiation from background sources.

In Miriam Manning & Carroll's (1957) study 373 mothers of children treated at Childrens Cancer Research Foundation were questioned by the same person. The age of the children ranged

Table 29.
(after Faber)

	No.		Therapy		Diagnostic irradiation over 40 (Therapy cases deducted)					
					before 5 yrs.		after 5 yrs.		Total	Total irradiation
	Total	above 40	No.	%	No.	%	No.	%	%	%
Chronic lymphatic leukæmia	283	278	5	1.8	23	8.4	22	8.1	16.5	18.0
Chronic myeloid leukæmia..	150	129	10	7.8	15	12.6	14	11.8	24.4	30.2
Acute leukæmia	395	163	13	8.0	13	8.7	26	17.3	26.0	31.9

from newborn to 14 years, and controls were taken at random from the Orthopedic Clinic, with the exception that cases from poliomyelitis were excluded. The results recorded are considered as preliminary by the authors.

Of the index children 187 suffered from acute leukæmia of unspecified type, and almost twice as many of their mothers had been exposed to therapeutic irradiation as mothers of children in the "other cancer" and "control" groups, or 19.5 per cent as contrasted to 11.9 per cent. This applied to all therapeutic irradiation prior to or during pregnancy with the index child. There was also a significantly higher incidence of allergic manifestations as hay fever, asthma, or hives in the histories of mothers of leukæmic children than in the other groups of mothers, and the authors think that this, if borne out in other studies, may give significant clues to the cause of leukæmia in children. Here it may be worth the while to recall that of the 36 mothers who had received irradiation 26 had received it for "dermatological conditions, usually acne", so that part of the correlation between allergy and leukæmia in this material might be related to allergic skin lesions.

It is pointed out by Manning & Carroll that, contrarily to the study by Alice Stewart, their study, begun before hers was reported, shows no association with roentgen irradiation for children with malignant diseases other than leukæmia. There was no difference in smoking habits between mothers of leukæmia children and other groups.

Faber (1957) in a preliminary report gives results from a study of 828 cases of leukæmia notified to the Danish Cancer Registry during the years 1950 to 1953, and selected as having clearcut diagnoses after reassessment of case records by the author. Thus, debatable cases in which the reporting hospital has made a positive diagnosis of leukæmia may in some cases have been excluded by the author, while other debatable cases, in which such diagnosis perhaps erroneously was not made will not enter the material. For these reasons it is not a material representative for the whole country, but on the other hand all cases will have been judged by the same person, even if this may mean some or other slight tendency to selection.

Only persons aged over 40 have been included, and for the purpose of the study on radiation the sexes are treated jointly, as it will appear from the table.

No attempt was made by Faber to study the amount of irradiations received at examinations at tuberculosis dispensaries, which will tend to reduce figures. The group who had received diagnostic irradiation was divided into cases in which irradiation had been given more than 5 years before the first symptoms of leukæmia and cases in which exposure occurred during the last five years.

The author finds that these preliminary results indicate that both chronic myeloid and acute leukæmia can be induced by irradiation, and that this is the case in some 13 per cent of the patients studied.

Table 30. (Sacks & Seeman).
Death Rates per 100,000 Population from Leukemia and Pseudoleukemia, United States, England and Wales, Canada, and Paris, 1931.

Age	United States*		England and Wales		Paris		Canada †	
	Male	Female	Male	Female	Male	Female	Male	Female
Under 5	3.71	2.97	3.03	2.35	1.34	—	1.84	1.88
5—14	2.16	1.33	2.69	1.48	3.81	2.26	1.34	0.73
15—24	2.18	1.32	2.36	1.31	2.72	0.81	1.41	1.35
24—44	3.33	2.35	3.35	2.03	2.89	1.49	2.02	1.56
45—64	7.42	5.43	5.83	3.98	4.12	3.27	5.19	3.16
65 and over	11.43	8.18	8.92	4.71	4.76	4.30	9.86	4.62

* White population only for the U. S. Death Registration States.
† Exclusive of Yukon and the Northwest Territories.
± Death rates at all ages have been adjusted for age and sex to the Standard Million Population of the U. S. Census of 1930.

EARLIER INTERNATIONAL COMPARISONS

It follows from the quantitative and qualitative reservations taken by most authors, and from the short period during which demographical statistics have been available on leukæmia and allied diseases, that only very few attempts have been made at international comparison of results in this field.

Sacks and Seeman (1947) in their paper previously quoted present death rates from United States Death Registration States, England-Wales, Paris and Canada for 1931. In order to arrive at a total death rate for each community, comparable in spite of differences in populations with respect to age and sex composition, the following adjusted death rates were computed; per 100,000 population: United States: Male: 4.09. Female: 2.85; England-Wales: Male: 3.75, Female: 2.29; Paris: Male: 3.22, Female: 1.83; Canada: Male: 2.75, Female: 1.82. The age distribution of rates is given in Table 30.

Sacks & Seeman who are well aware of the limitations of their material conclude that when it is remembered that procedural variations in cause-of-death classification exercise an influence in international comparability of mortality statistics, the small differences in these observed rates indicate a very similar experience in each of the communities studied. However, the sex ratio of rates showed some variation: For U. S. A. the death rate for males was 43 per cent greater than for females, and for Canada 51 per cent, while England-Wales showed 64 per cent and Paris 76.

Hewitt (1955) brings the following table based on official mortality statistics of the various countries and W. H. O.

In the evaluation of the international differences appearing from the table, Hewitt points out that the ratio of myeloid to lymphatic cases was higher in Scotland than in England-Wales, which feature he relates to the apparent tendency for the Scottish death rate to be relatively high during the middle part of life, when the proportion of myeloid cases is highest. In Northern Ireland he finds a clear excess of leukæmia deaths between the ages of 35 and 54 chiefly occurring among men. For Eire, where rates were low the greatest deficit in "expected" deaths was in the oldest age group.

With regard to U. S. A. Hewitt finds rates for individuals who were past working age two to three times higher that in England, which to him suggests the possibility of a difference in diagnostic standards at least in elderly patients. Hewitt seems puzzled by the finding that despite the very low rates for non-whites at each extreme of life, the mortality ratio for coloured persons in the age group 35—44 was even higher than for white Americans. However, with the information on hand he suggests the significance of social factors, later supported by MacMahon, and Koller, and Clark.

Also for Germany rates are low for the very young and very old, but the author seems most impressed by the figures from Denmark, which, however, he has taken from mortality material only: "Here the population is considerably smaller than that of Scotland" (Scotland: 4.8 mill., Denmark: 4.3 mill.) "yet had as many deaths from leukæmia in 2 years as did Scotland in 3 years. This country provides the most challenging example so far revealed of a geographical differential in leukæmia. In environmental and social conditions Denmark must more closely resemble Britain than it does the United States. Yet in Denmark leukæmia mortality is approximately equal to that in the United States. The payment of a notification fee for cases of leukæmia may stimulate Danish physicians to make the diagnosis in cases where it would have been overlooked by a British doctor, but this seems unlikely to provide the full explanation." Apparently the latter remarks refer to the token fee for notification of cases to the cancer registry, which is equivalent in value to about 1 shilling. Hewitt concludes:

Table 31. (Hewitt).

Leukaemia Mortality in Certain Countries, Expressed as Percentage of Contemporary Mortality in England and Wales, Standardized for Age and Sex.

Country	Period	All Ages Combined			Sexes Combined, by Age Group													
		Persons	Males	Females	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-
Scotland	1950–52	96	94	98	92	97				104				102		86		99		91
Northern Ireland	1950–52	86	86	85	95			90				140					55			
Eire	1950	64	65	63	84			71					61				48			
U.S.A. White	1949–50	153	153	152	129	129	94	109		136		143		151		195		306		
U.S.A. Non-white	1949–50	83	85	80	57	64	70	85		140		102		109		63		56		
Germany	1948	88	90	85	74	88	107			94			99			89		56		
Denmark	1951–52	147	151	141	121	96	122						137				200			219

"For example the gross excess of leukæmia in Denmark by comparison with neighboring Germany must be attributed to something more specific than the general standard of living. It is not impossible that the higher rate in Denmark may have arisen from an exceptionally wide use of radiography and radiotherapy".

To the present authors it does not seem unlikely that for some reason or other the diagnosis of leukæmia may be made relatively more often in Denmark than in Scotland, but we are inclined to believe that this may be due to other factors than the economic, and that for instance the reasons suggested by Hewitt for the higher rates in U. S. A. than in England, for elderly patients may also apply to Denmark. As to Danish diagnostic standards we would refer to the tables of the present and earlier publications from this Registry (1949, 1952) giving the rate of hospital diagnoses for various age groups. For the medical use of radiation we may refer to Faber (1957), but finally we should admit that radiography by unskilled personnel, like assistants in shoe-shops, is still allowed in Denmark, where, however, the control of the medical usage of radiation is very sharp. On the other hand the damage done by such unmedical usage of ionizing radiation will be difficult to assess, and will mostly have been forgotten by patients questioned on this point.

For lymphogranulomatosis an international comparison of rates was recently attempted by MacMahon (1957) mainly on the basis of the three materials of 1) Uddströmer's 536 cases from Sweden 1915—31 (p. 76), 2) Dorn & Cutler's 385 cases from ten metropolitan areas of the United States, 1947 (1955), and 3) 392 cases from Danish morbidity statistics for 1943 to 1947 published by Clemmesen, Busk & Nielsen (1952). To this MacMahon adds 546 case records of white Brooklyn residents treated during the period 1943 to 1952 in 34 Brooklyn hospitals, supplemented with case records from hospitals in other boroughs of New York City and with death certificates for Brooklyn residents dying within this area. When clinical records were found only patients for whom the diagnosis was supported by biopsy or autopsy were included in the series. The white population of Brooklyn averaged 2,540,828.

It is MacMahon's thesis that the age distribution of incidence rates for Hodgkin's disease forms a distinctly bimodal curve with one peak for the age group 25 to 29, and a second for the 70 to 74 year group. This, he finds, applies to the materials mentioned, and also for mortality rates for the United States he finds the curve definitely bimodal, although the first mode is less distinct than in the curve for the Brooklyn data. Finally, MacMahon surveys death rates for a number of countries taken from the publications of the World Health Organization, and computed for both sexes together.

In principle the present authors would be disinclined to discuss irregularities in age distribution curves covering both sexes at one time. The

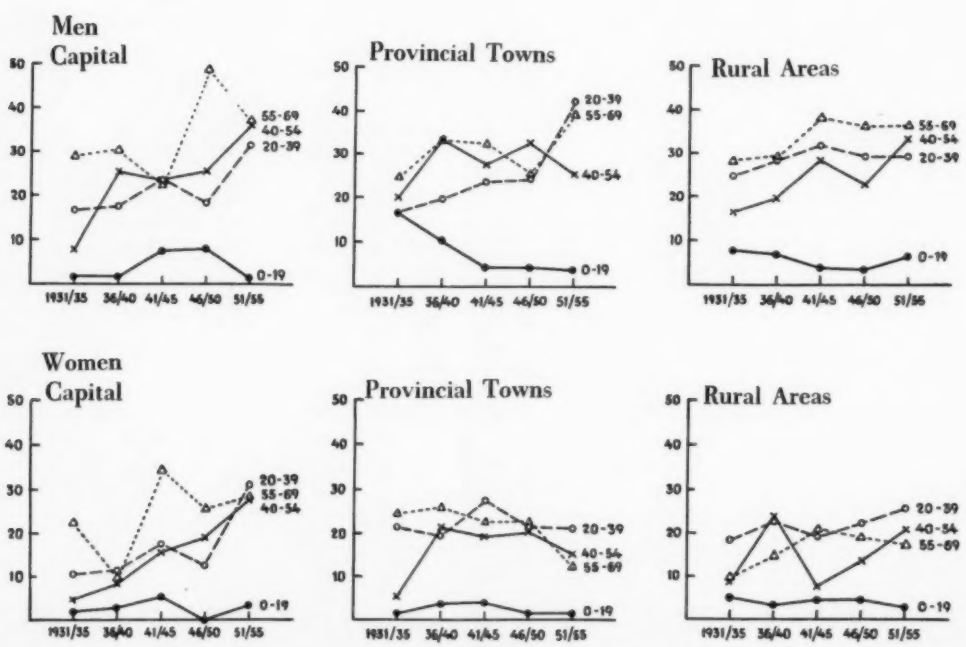


Fig. 9.
Lymphogranulomatosis (Hodgkin).

justification of this attitude, as far as lymphogranulomatosis is concerned, may appear from Fig. 11 which for most countries shows different age distribution of mortality rates for the sexes; consequently the material will not be homogenous with regard to the quality studied, if the age distribution is examined by means of one combined material. Also, it may need some amplification when stated by MacMahon that "bimodal age-incidence curves are unusual and suggest either that different etiological mechanisms are operating at different periods of the age span, or that different disease entities have been incorporated in the original classification". Any factor, which at some particular age period, for instance the climacterium, might tend to delay or forward the onset of disease, perhaps only in a fraction of the cases under study, may well cause a bimodal age -incidence curve, so that the term "etiological mechanism" should be taken as covering pathogenesis as a whole.

With regard to the actual question, we have tried to confirm the existence of a bimodal curve for the age distribution of death rates from Denmark, realising fully, that MacMahon found the trend in this direction less pronounced for material on mortality. As it appears from Fig. 9 we did not find evidence for the assumption that curves for some age groups would regularly take a lower course than others, except for the very young.

In comparison with the morbidity materials for ten cities in the United States, and for Brooklyn white residents, our material for men in Copenhagen rather suggests a more pronounced drop in incidence rates between ages 43 and 57 than any of the two other curves.

However, if we consider the small number of patients, and the protracted course sometimes

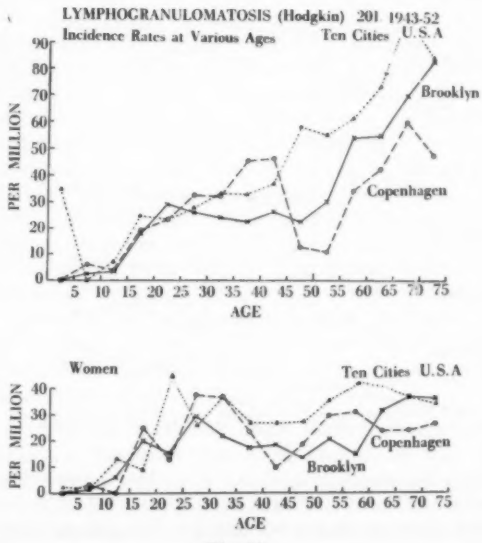


Fig 10.

taken by lymphogranulomatosis it would to us seem perfectly possible that some event causing earlier biopsy of a lymph node in even a small number of cases might easily explain the shape of this curve, and we believe that most readers will find this confirmed by the figures in Table 386 P. 113. On the other hand we are in full agreement that the age curve for Hodgkin's disease tends to show a shape quite different from those of most other malignant disease.

Nevertheless, we cannot follow MacMahon fully when in comparing figures for persons in the various countries he makes it a point that because the histological and clinical picture of Hodgkin's disease will change with advancing age, the age curve suggests that this name in reality covers two different diseases or etiological entities. MacMahon points to the similarity between the histological pictures of Hodgkin's sarcoma — a histological variety of lymphogranulomatosis — and reticulum-cell sarcoma, and he mentions that this picture occurs almost solely among those in the age groups more than 40. Next, the author points to the similarity in the shape of the age curve for the oldest age groups between Hodgkin's disease and reticulum-cell sarcoma: "the similarity of the two curves in the second half of life is remarkable, since even between known neoplastic disorders, differences in shape and slope of the age incidence curve are usual."

From our experience in Cancerregisteret, from where age distribution curves are as a rule plotted on identical scale (Clemmesen & Nielsen, 1952), we are inclined to believe that such differences between age curves are less frequent and less pronounced than generally assumed, and that

Table 32. (MacMahon).
Death Rates from Hodgkin's Disease in Selected Countries, 1950 to 1952.

Country	Death rate per million*			Percentage U.S. rate		
	Age 0—39	Age 40 & more	All ages	Age 0—39	Age 40 & more	All ages
United States (white)	9.9	32.6	18.1	100	100	100
Canada	8.7	29.1	16.0	88	89	88
Denmark	15.0	25.7	18.8	152	79	104
Finland	9.5	21.5	13.8	96	66	76
Norway	11.4	22.8	15.5	115	70	86
Sweden	7.9	22.6	13.2	80	69	73
England & Wales	10.1	25.0	15.4	102	77	85
Ireland	9.5	27.8	16.1	96	85	89
Scotland	10.7	30.2	17.7	108	93	98
France	10.1	20.6	13.9	102	63	77
Germany	9.0	21.7	13.6	91	67	75
Netherlands ..	17.6	23.7	19.8	178	73	109
Italy	10.7	31.1	18.0	108	95	99
Switzerland ..	12.9	25.7	17.5	130	79	97
Australia	5.9	21.5	11.5	60	66	64
Japan	1.8	13.3	5.9	18	41	33

*) Within each broad age group all rates have been standardized to the distribution of the United States white population in five-year groups.

differences are easier to demonstrate with certainty for the classes of younger age, in which the general population will be more numerous, and consequently the age curve more reliable than for the older age groups; also the numerical frequency of the disease in question will be of considerable importance to the reliability of curves.

MacMahon ends by writing that the high rates for lymphogranulomatosis in the first half of life "in the three traditional dairy-producing countries (Netherlands, Denmark, and Switzerland) are provocative and warrant further investigation." The present authors would be inclined to look for other similarities of medical significance between the said three thrifty and highly organized small European nations, than the production of dairies, for the significance of which to the incidence of Hodgkin's disease we shall with interest await scientific evidence.

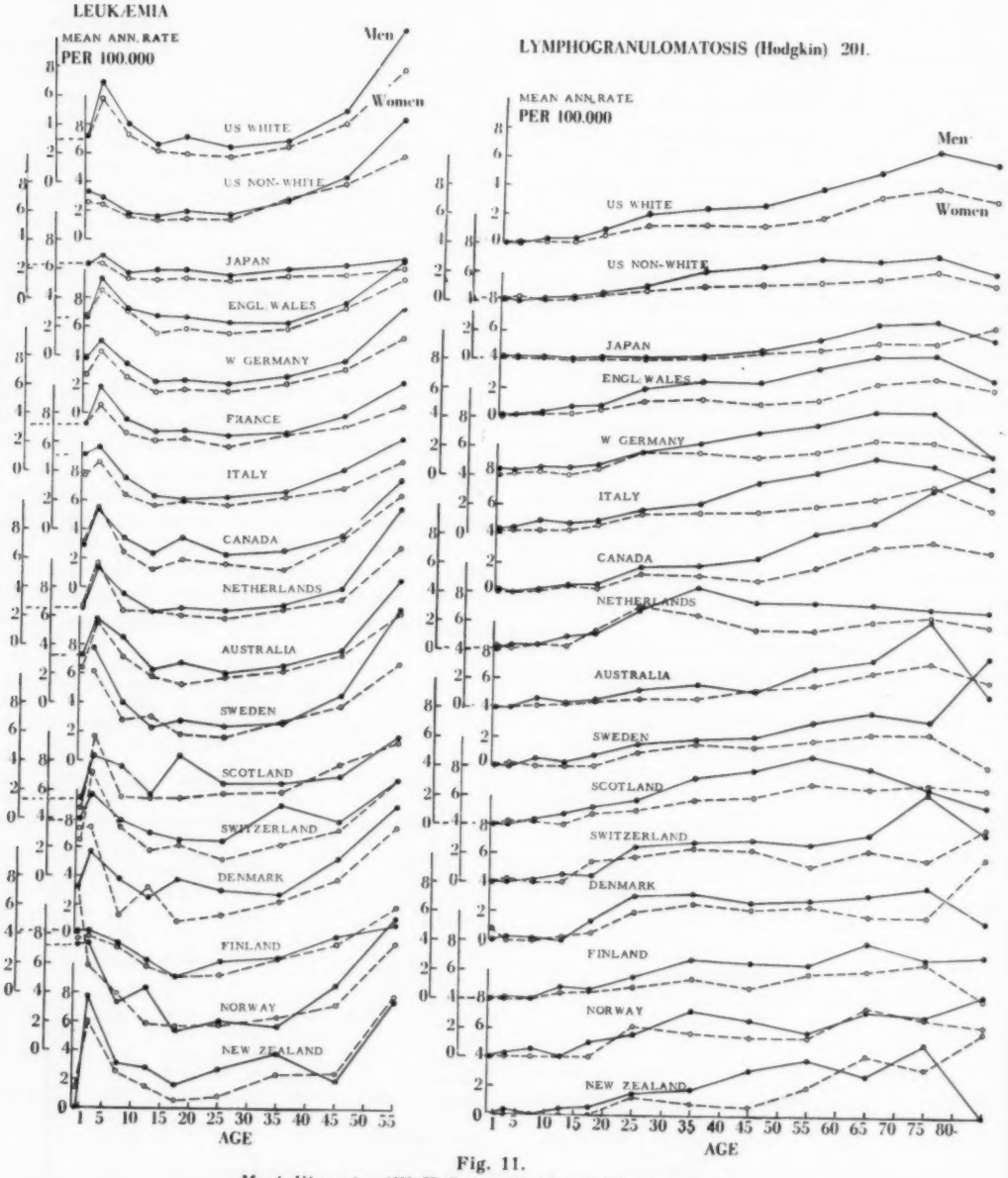


Fig. 11.
Mortality rates (W. H. O Arn. Epid. Vital Statist. 1953).

It should be noticed that when the reader starts from the bottom, the first curve refers to the ordinate scale to the right, the second to the intermediate ordinate scale, and the third to the left scale — and so forth —.

INTERNATIONAL COMPARISON BASED ON RECENT FIGURES

At the present stage of development in the therapy of leukæmia and lymphogranulomatosis, it seems unlikely that international differences in the efficiency of treatment would cause more than the effect of a prolongation of the disease on the age curve of certain countries, while differences in the efficiency of diagnosis may perhaps be expected to influence the rates of various countries. For these reasons, a thorough study of international differences in incidence of the diseases in question would require collection of information directly from the countries concerned, but for an orientation we shall present a series of curves illustrating the age distribution of mortality rates, drawn on the basis of the report from the World Health Organization, 1955.

Fig. 11 shows mean annual mortality rates at various ages for "leukæmia and aleukæmia" in a number of countries for the years 1952 to 1954. Rates are given only up to the age group 50—59 inclusive, because older age groups show pronounced irregularities, analyzed separately in Figs. 12—14.

Up to the age of 59 curves are remarkably alike for the various countries, with the exception of Japan, where the gradual increase after the age of 25, seen in most countries, seems absent, which would be difficult to explain through the absence of lymphatic leukæmia, since according to Figs. 36—39 both myeloid and lymphatic leukæmia will increase in incidence between 25 and 55 years if we are to judge from rates for Copenhagen or Brooklyn.

On the whole, rates for men are higher than for women, and, in contra-distinction to most other malignant diseases, children in the first years of life show relatively high rates. This seems most pronounced for the Scandinavian peninsula, both in Norway and in Sweden, while a similar trend appears for adjacent Finland. It should be added that Swedish figures have not been worked out separately for the first year of life. It is instructive that Danish girls should show a rate of 7.3 in the first year of life against a rate of 3.3 for boys. Similarly, the corresponding rates for Norway is 11.3 for girls and 7.3 for boys. The problems about rates for the first years of life are discussed on pages 83 and 104 but it should be mentioned here, that for Denmark the rates for other years do not quite bear out the sex proportion given, which must be ascribed to the small numerical values cf. Table 33.

While the relatively high rates for newborn children has been discussed earlier, it may be unexpected that in a number of countries there seems to be a very slight upward trend for rates between the ages 15 and 20 years, most evident for Scotland, Canada, and U. S. Whites. The constancy of this slight trend seems to confirm its reality, but most other countries than the United States would probably give numbers too small for a detailed analysis.

Table 33.
Deaths from Leukæmia and Aleukæmia, Danish Health Service.

	Boys		Girls	
	0-1	1-4	0-1	1-4
1950	1	12	3	14
1951	2	9	2	11
1952	1	8	3	11
1953	2	12	—	—
1954	3	11	4	14

The diagram for lymphogranulomatosis Hodgkin shows a uniformity of curves similar to that of leukæmia curves, and with a more pronounced excess for men. Also here the curve for Japan differs from the others, and it might perhaps be tempting to relate this to the absence of lymphatic leukæmia in that country.

As it will appear from Figs. 12—14 the international differences are more pronounced among the old than at any other age. The curve for all Denmark shows a drop for the oldest age group, deeper than in the curves for Copenhagen (Figs. 22—25), why we are inclined to ascribe it mainly to less thorough examination of old people in rural areas. Similar factors may influence rates for old people elsewhere.

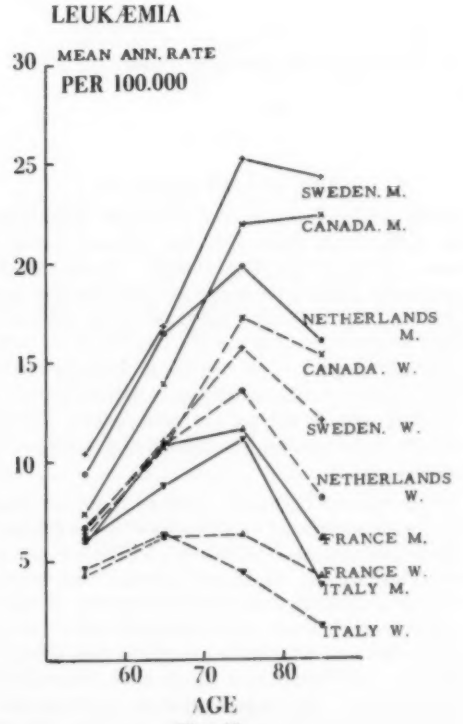


Fig. 12.

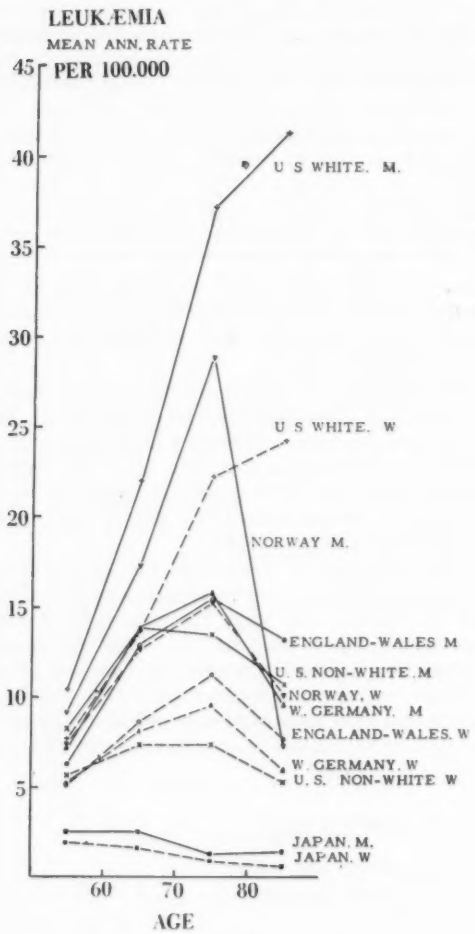


Fig. 13.

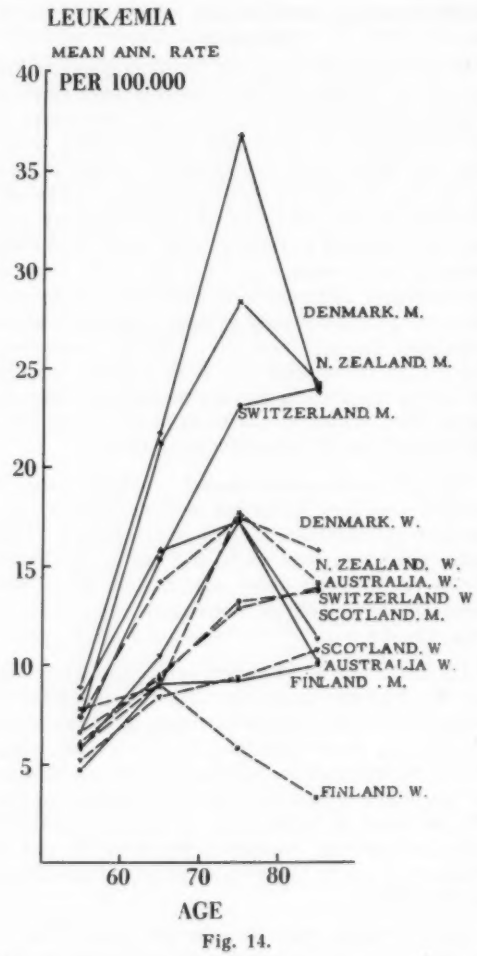


Fig. 14.

NEW DANISH MATERIAL

The major part of the material presented in the tables and figures of the present paper has been collected by The Danish Cancer Registry under the National Cancer League, for the period 1943 to 1953 inclusive, although most tables have been worked out only for the two five year periods 1943—1947 and 1948—1952. It is believed that this material will represent, as accurately as it is possible, the incidence of new cases diagnosed within metropolitan Denmark for the period concerned.

The Cancer Registry receives from all Danish hospitals voluntary notifications on all cases of malignant diseases admitted, including all cases of leukæmia and Hodgkin's disease and, irrespective of malignancy, all cases of brain or bladder tumours. For each case notified, and for each diagnosis later announced as discarded, a token fee of 1 kr., equivalent to 1 sh. is paid. Subsequently, notifications are supplemented with copies of death certificates, which all pass the Registry. This system is based on the assumption that in Denmark no case of malignant disease will be cured without passing a notifying hospital — an assumption which may not apply to all countries. It is an advantage that the population covered is small and well delimited, and that the medical facilities are uniform and good.

All details of this system have been recorded in the present journal by C l e m m e s e n (1956), together with full details on the population at risk. A full survey of the scientific activities of Cancerregisteret, with full bibliography of its rather scattered publications up to medio 1957, will be found in "Cancer" by R a v e n, Vol. 3 (1958). Our new material is given in detailed tables on Pages 109—122.

Lymphogranulomatosis.

The changes in the nomenclature applied in the international system for registration of deaths, which in many countries have reduced the possibilities for evaluation of changes in rates over

longer periods, have not affected the working tables of the Danish Health Service on which the following diagram has been based:

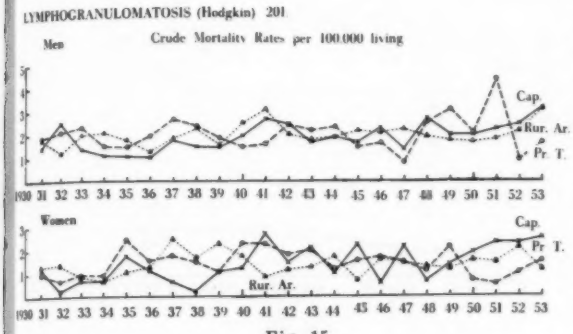


Fig. 15.

As malignant neoplasia lymphogranulomatosis is outstanding in showing almost no difference in level of crude mortality rates for Danish capital, provincial towns and rural areas, nor is there any indication of changes in rates between 1930 and 1953, and the same impression is gathered from a diagram of crude incidence rates for the period of function of Cancerregisteret:

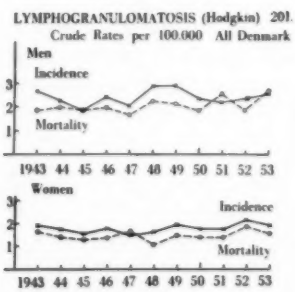


Fig. 16.

These impressions of constancy of values have, as necessary, been confirmed for single age groups by the analysis given in Fig. 9, which displays no trend in the oscillations in mortality rates from 1931 to 1955, an observation well in keeping with Shimkin's experience from U. S. A., illustrated in Fig. 6, which showed a proportionate increase in rates for all age groups.

It is true that constancy in rates of various kind suggests a high degree of uniformity in incidence and reliability of diagnosis but it is difficult to see why these qualities should be more pronounced for Hodgkin's disease than for many other malignant diseases. A survey of age distribution curves for incidence rates in Danish capital, provincial towns and rural areas (Clemmesen & Nielsen 1952) shows that while some cancers show somewhat higher rates for all ages in the capital than in other towns or rural areas, nearly all malignant tumours show definitely higher rates for old persons in towns, particularly the capital, and this seems to apply whether a difference for younger groups exists or not. The explanation nearest at hand is, that in the city of Copenhagen the diagnosis is made with more efficiency among the old than elsewhere in the country.

On this background it is easy to understand that a disease like Hodgkin's with its nearly horizontal age curve — that is, with far lower incidence rates among the old than most cancers — in contradistinction to most other malignancies will show high uniformity of rates between areas where the efficiency of diagnosis among the old is varying.

LEUKÆMIA

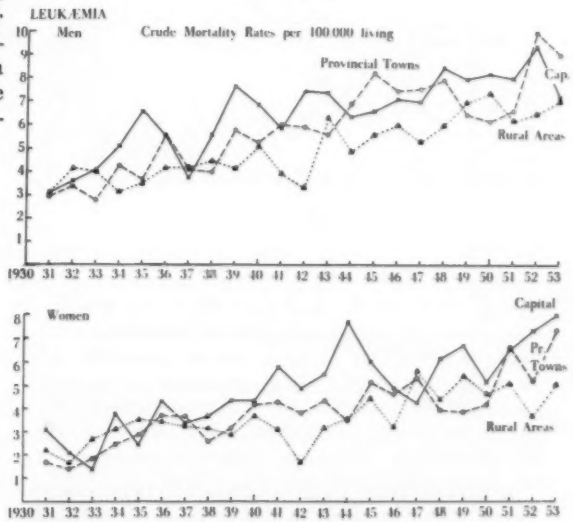


Fig. 17.

A diagram of rates since 1931, taken from the tables of the National Health Service suggests that a tendency to higher mortality in the capital than in other habitation areas, which may have been present for men previously, was developed or accentuated for both sexes about 1939, to diminish again about one decade later. This difference was examined in 1952 by Clemmesen, Busk & Nielsen, who ascribed it to diagnostic improvements associated with the introduction of sternal marrow examinations, which will probably have spread gradually from the capital into the country.

A comparison of crude incidence and crude mortality rates shows no traces of this rise dur-

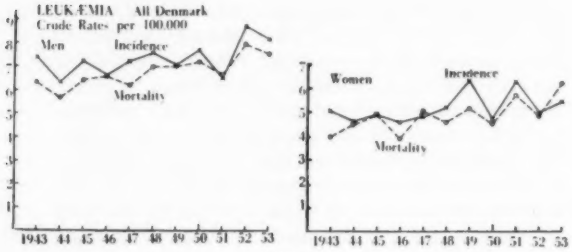


Fig. 18.

ing the period of the Cancer Registry, i. e. since 1943.

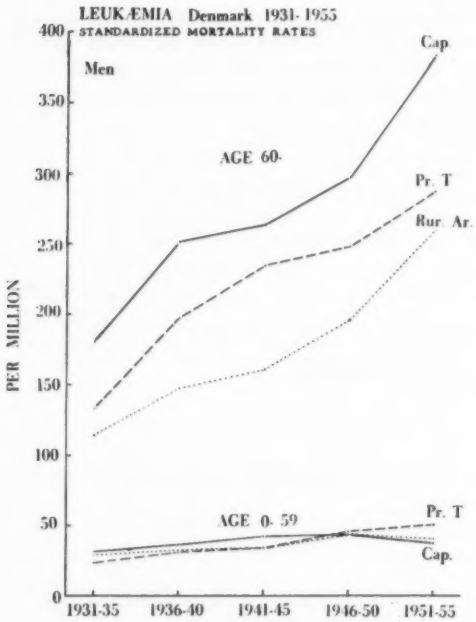


Fig. 19.

It appears from diagrams 19 and 20 that persons below 60 contributed to the increase in national rates only with a modest rise up to 1940, which may well have been due to general improvements in diagnostic technique during this period, while the major part of the increase occurred among the old. This corresponds closely to S h i m k i n's experience from the United States illustrated in Fig. 6, but is difficult to reconcile with H e w i t t's suggestion that the higher rates for Denmark than for Scotland should have arisen from an exceptionally wide use of radiography and radiotherapy. Were we to accept this view, we would have to assume a longer latent period for actinigenic leukæmia than usual supposed, like the long latent period known from the actinigenic bronchial carcinoma from Schneeberg, or the bronchial carcinoma caused by cigarette smoking. Furthermore, this long latency would

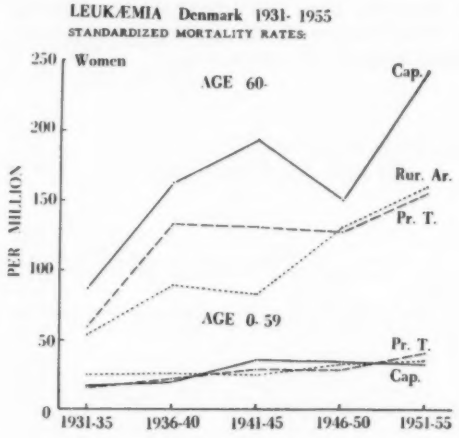


Fig. 20.

have to be applied mainly to the lymphatic leukæmia, which is the prevalent form among the old, although usually not ascribed to actinic effect.

As an illustration of the development we bring the age distribution of mortality rates for women in rural areas of Denmark for the period 1931 to 1955, which is the clearest of the diagrams on this question.

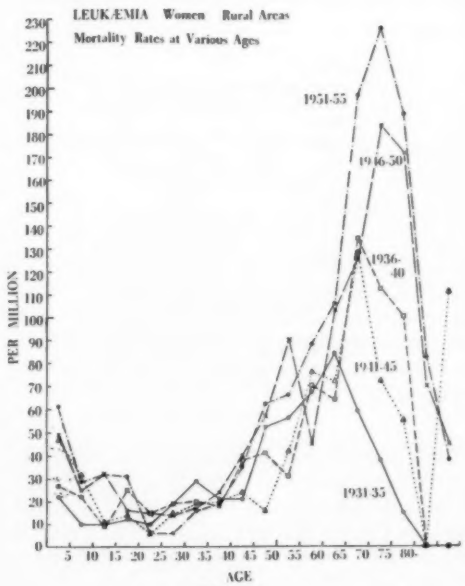


Fig. 21.

The factual incidence of the various forms of leukæmia will appear from Figs. 22 to 25. From Tables 37 a and 38 a it will be seen how many cases were not specified according to type.

It appears from the diagrams on lymphatic leukæmia that the incidence of this disease is roughly the same in capital, provincial towns and rural areas up to the ages over 60 years when the

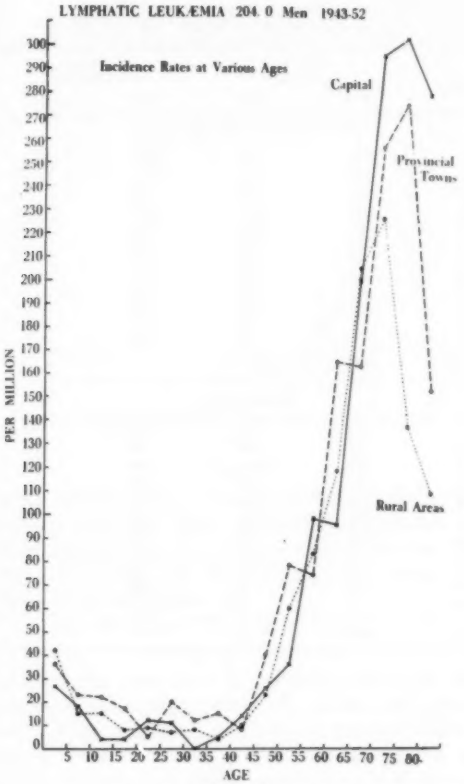


Fig. 22.

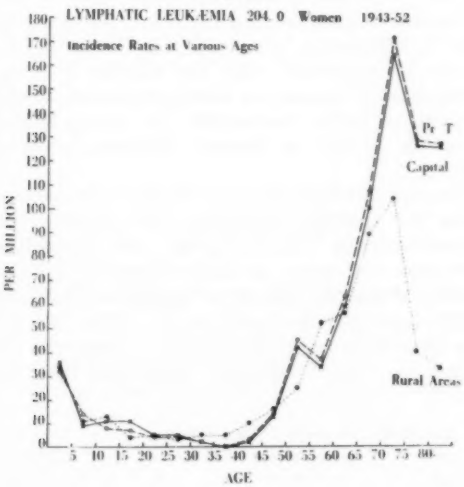


Fig. 23.

capital shows rates far beyond those for rural areas, and the same applies to myeloid leukæmia. In evaluating the curves in the old age groups, it should be remembered that the high incidence rates apply to age groups rapidly diminishing in size.

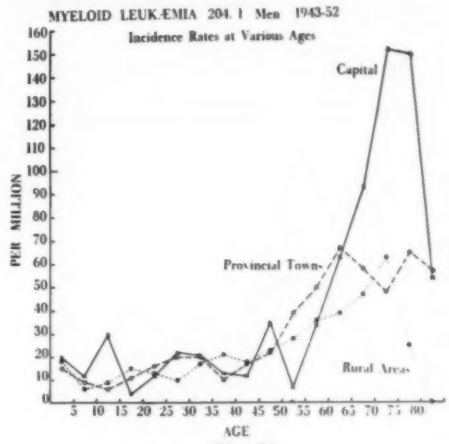


Fig. 24.

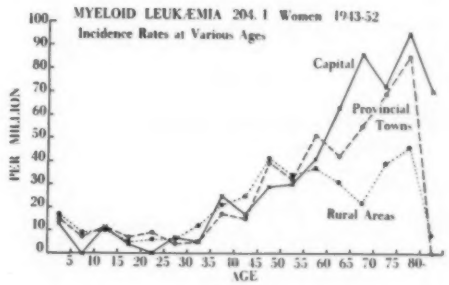


Fig. 25.

LEUKÆMIA IN CHILDREN

Hewitt (1955) and A. Stewart (1957) have pointed to steadily increasing mortality rates for leukæmia among children in England, where boys show somewhat higher rates than girls do (Fig. 8), where lymphoid leukæmia seems to be the prevalent type, and where the question of a causation through roentgen irradiation of mothers is under examination. Considering the diagnostic difficulties in cases of anaplastic type, and the possibility that children may respond to irradiation with lymphatic leukæmia more often than adults are supposed to do, we find it difficult to arrive at conclusions from the information available. However, in Denmark some features of development mutual to children and adults may be of interest.

From the material of Cancerregisteret for 1943 to 1952 there is no reason to assume a difference in incidence rates between boys and girls, and some of the differences in sex ratios appearing from the material of the World Health Organization reports may be due to short-termed oscillations in rates for these rare diseases. The interrelation between rates for leukæmia and other malignant diseases of childhood seems fairly clearly illustrated in Fig. 26.

Incidence Rates at Various Ages Denmark 1943-52

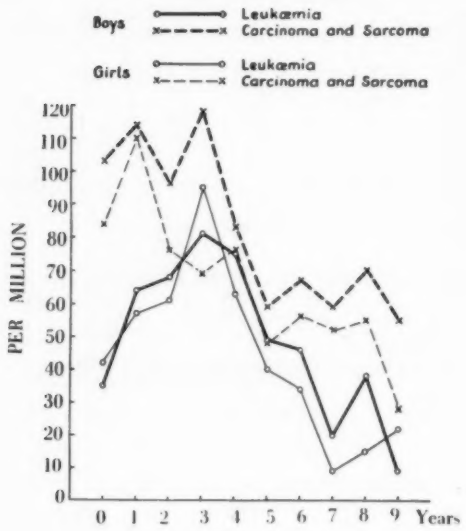


Fig. 26.

LEUKÆMIA Denmark 1931-55
Mortality Rates

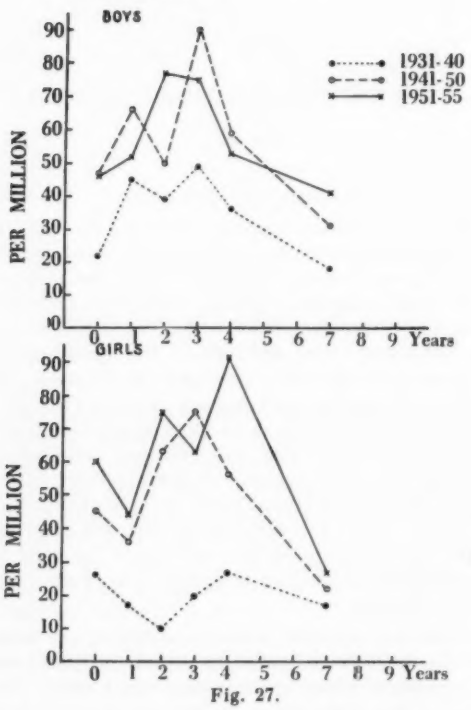


Fig. 27.

A comparison of mortality rates computed on the basis of the tables of the Danish Health Service for the years 1931 to 1955 tends to show an increase in rates for boys and girls from 1931 to 1940, or during the period in which the increase in rates involved adults both younger and older

Table 34.
Cancerregisteret Denmark 1943—52.
Cancer in Children under 10 years.

Age Years	Absolute numbers		Incidence per 1.000.000	
	Boys	Girls	Boys	Girls
	Carcinoma and sarcoma.			
0	44	34	103	84
1	48	44	114	110
2	40	30	96	76
3	48	27	118	69
4	33	29	83	76
5	23	18	59	48
6	25	20	67	56
7	21	18	59	52
8	24	18	70	55
9	18	9	55	28
Total	324	247		
	Leukæmia.			
0	15	17	35	42
1	27	23	64	57
2	28	24	68	61
3	33	37	81	95
4	30	24	75	63
5	19	15	49	40
6	17	12	46	34
7	7	3	20	9
8	13	5	38	15
9	3	7	9	22
Total	192	167		

than 59 years, although it was most pronounced among the older. However, when the increase in rates ceased among the younger of the two age groups about 1940, it seems to have ceased also among the children, while it continued among the old, presumably because diagnosis could still be improved upon among the aged. We therefore find it difficult to believe in any continuous increase in leukæmia rates for Danish children, which speaks against an actinic causation in any number of cases measurable in demographical statistics, as far as Danish children are concerned.

The age distribution of incidence rates for both sexes for multiple myeloma, for lympho- and reticulosarcoma and for other and unspecified sarcomas will serve as background for the estimation of Danish figures for malignant neoplasias of the hæmopoietic tissue proper (Figs. 28—33). The general shape of the curves is more like diagrams for other malignant neoplasms than like

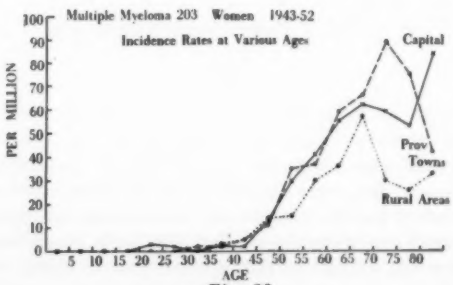


Fig. 28.

OTHER HÆMOPOIETIC NEOPLASIAS

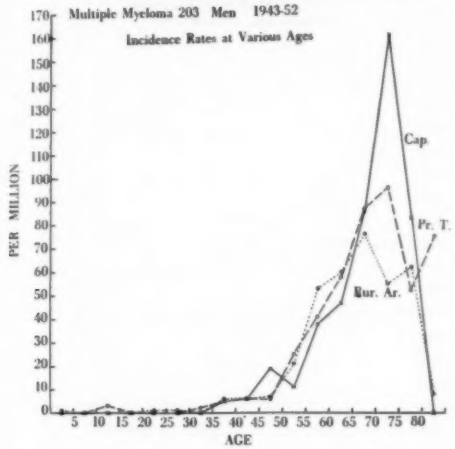


Fig. 29.

those for Hodgkin's disease. Rates for the capital exceed rates for other habitation categories considerably for old age groups, while rates for rural areas are generally lower than for towns, also for groups of middle age.

Fig. 30.

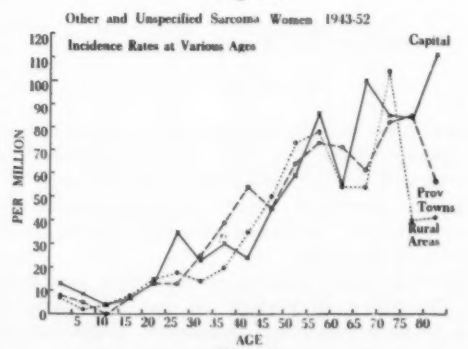


Fig. 31.

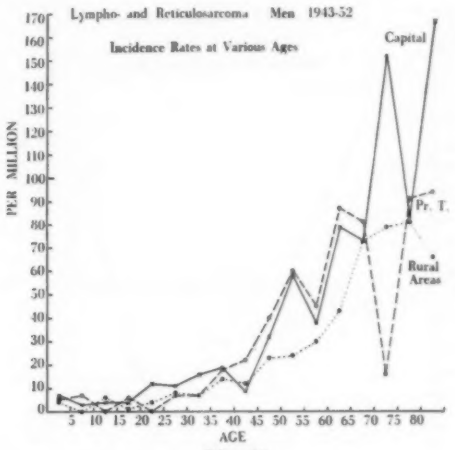


Fig. 32.

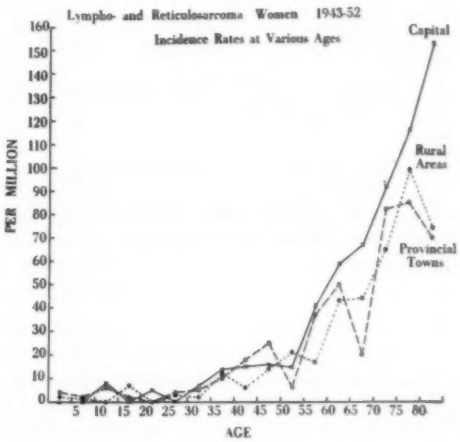


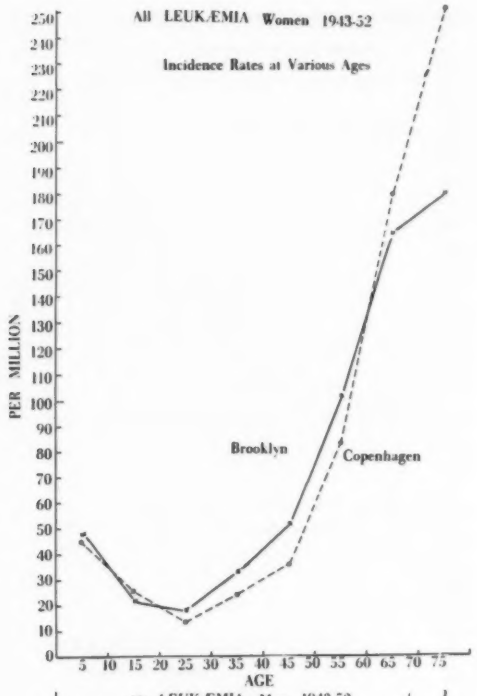
Fig. 33.

Comparison Copenhagen-Brooklyn.

The material published by Mac Mahon, Clark and Koller on incidence of leukæmia and lymphogranulomatosis in Brooklyn represents the only opportunity for comparison directly with the Danish morbidity data, in particular for Copenhagen. We have therefore drawn diagrams plotting incidence figures for both townships together, realizing that differences in clinical definitions may in some cases exert an influence difficult to assess.

It is evident from the diagrams on All Leukæmia that the shape of the two curves is largely the same, and that there is some tendency for Brooklyn rates for middle-aged groups to exceed those of Copenhagen. However it may be noted that the rate for the oldest age group in these, like in all other diagrams except for acute leukæmia is highest for Copenhagen thus suggesting a more close examination of old people in Copenhagen than in Brooklyn.

Since it would be expected a priori that the material from Copenhagen would have a better



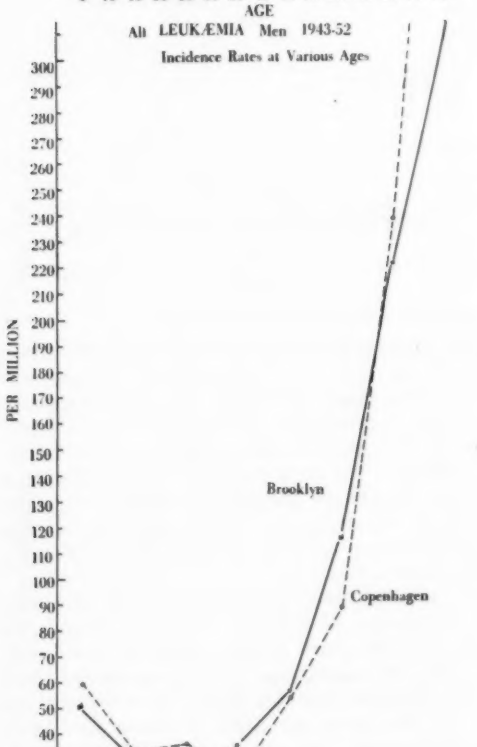


Fig. 34 and 35.

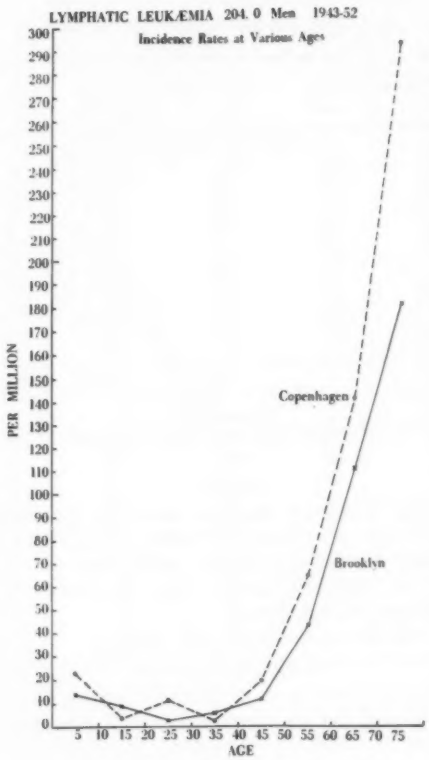


Fig. 36.

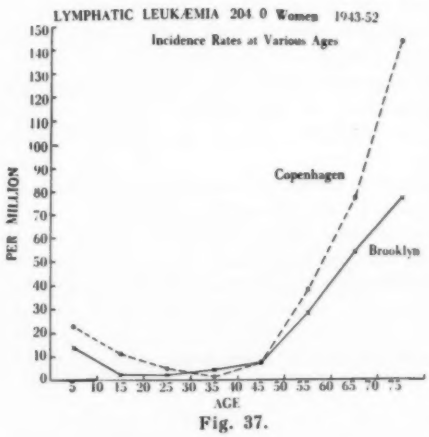


Fig. 37.

chance to cover all patients with leukæmia than the material from Brooklyn where a number of patients may be lost, going out of the borough for treatment elsewhere, there is every reason to believe that the difference is more pronounced than illustrated here.

A further analysis based on the details available, and illustrated in Figures 36 and 37, tends to show higher rates for lymphatic leukæmia in Copenhagen than in Brooklyn.

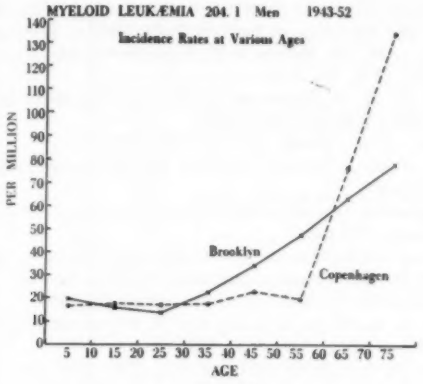


Fig. 38.

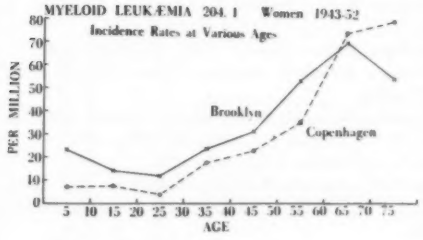


Fig. 39.

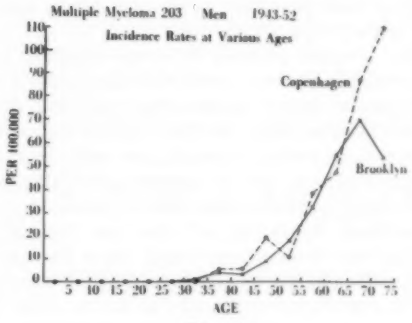


Fig. 40.

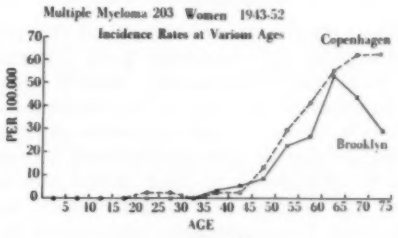


Fig. 41.

Contrarily, for myeloid leukæmia rates are higher for Brooklyn, in the age groups that count by weight of numbers, as seen in Figs. 38 and 39.

It is with some reservation that we bring the figures in Table 35 illustrating the age distribution of incidence rates for leukæmic diagnoses signified as chronic or acute, because these terms may not be applied to the same categories of diseases in the two towns, quite apart from the fact that these designations are not systematically applied in all notifications, at any rate as far as Copenhagen is concerned. It appears however that the age distribution is similar for the two sexes and the two towns.

On the whole it would seem probable that the differences in incidence rates for leukæmia between Copenhagen and Brooklyn are mainly due to a larger number of cases characterized as acute in Brooklyn. Since for all other categories rates for the old age groups are highest in Copenhagen,

Table 35.

Incidence Rates of Leukæmia 1943–52 per million.
Brooklyn and Copenhagen. Mac Mahon and Cancerregistret.

AGE	Lymphatic leukæmia		Myeloid leukæmia		All leukæmia		All chronic leukæmia		All acute leukæmia		Chronic lymphatic leukæmia		Chronic myeloid leukæmia	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Brooklyn														
0— 9	14.1	13.7	19.7	23.1	50.4	47.9	5.5	4.2	44.9	43.7	.0	.5	1.5	.5
10—19	9.3	2.3	15.7	14.0	31.4	22.2	2.9	4.1	28.5	18.1	.0	.0	2.3	2.3
20—29	3.0	2.3	13.8	11.9	17.8	18.3	7.4	5.1	10.4	13.3	.5	.5	6.9	3.7
30—39	6.0	4.6	22.1	23.6	35.2	32.6	20.1	11.8	15.1	20.8	4.0	3.2	11.6	7.7
40—49	11.9	7.8	34.0	30.9	55.1	50.8	34.1	27.3	21.1	23.6	10.3	6.8	17.3	14.7
50—59	43.6	28.7	47.6	52.8	116.4	100.8	83.9	55.4	32.4	45.4	40.3	18.7	28.4	25.4
60—69	110.5	54.0	63.1	69.3	221.0	163.2	172.6	111.1	48.4	52.0	101.0	52.0	37.9	32.6
70—	180.7	77.4	78.0	53.4	316.7	178.8	265.4	128.9	51.3	49.8	167.3	70.0	53.5	27.6
Copenhagen														
0— 9	22.9	22.9	16.2	7.0	59.4	45.0	28.3	23.9	31.0	21.1	12.1	12.7	8.1	2.8
10—19	3.8	11.0	17.3	7.3	32.7	25.6	15.4	16.5	17.3	9.2	1.9	7.3	5.8	7.3
20—29	11.3	4.9	17.0	3.6	35.7	13.4	24.0	9.7	11.3	3.6	7.1	2.4	9.9	3.6
30—39	2.7	1.1	17.4	17.4	22.8	24.1	18.7	18.3	4.0	5.7	2.7	1.1	14.7	12.6
40—49	19.8	7.6	22.8	22.8	53.3	35.4	39.6	31.6	13.7	3.8	15.2	7.6	18.3	20.2
50—59	64.7	38.2	19.6	35.0	88.2	82.8	80.3	63.7	7.8	19.1	62.7	36.6	15.7	23.9
60—69	141.1	77.8	76.4	73.4	238.0	179.3	223.3	162.0	14.7	17.3	135.2	75.6	73.5	64.8
70—	292.7	144.0	133.9	78.2	481.2	250.4	451.5	244.1	39.7	9.4	277.8	144.0	119.1	68.9

it is likely that Brooklyn rates as a whole are in reality higher than illustrated.

To the present authors it seems unlikely that more comparisons can profitably be carried out without more direct comparison of local diagnostic technique. Such medical assessment would seem necessary before attempts are made to carry out statistical tests on the statistical significance of differences. On the other hand, it would seem that medical standards of the two townships Brooklyn and Copenhagen must have reached a considerable degree of comparability if we compare the age distribution of incidence rates for multiple myeloma in the two conurbations.

SUMMARY

Available evidence of demographical character on the mortality and morbidity from malignant neoplasias of the hæmopoietic system among various populations or parts of populations have been critically reviewed, with quotation of figures and tables. It appears that international differences must be considered in light of the fact that the oldest age groups, in which incidence rates are most often high, will often not benefit from progress in diagnostic technique until at a rather late stage of development. This seems to explain a number of international differences in apparent mortality rates for leukæmia, although Japan, for instance, seems to form an exception.

Contrarily, the absence of a pronounced rise in the age curve for lymphogranulomatosis will favour uniformity of rates between countries.

As far as Denmark is concerned the high total rate for leukæmia is largely due to high rates for the oldest age groups, and this applies also within the country itself as an explanation of higher crude rates for the capital, and other towns than for rural areas.

Rates for children have ceased to increase in Denmark, and there is no evidence of actinigenic cases in any number likely to affect demographical statistics.

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Table 36.

Danish Health Service. Leukæmia Mortality Rates at Various Ages per 100.000.

Age	Capital					Provincial Towns					Rural Areas				
	1931—35	1936—40	1941—45	1946—50	1951—55	1931—35	1936—40	1941—45	1946—50	1951—55	1931—35	1936—40	1941—45	1946—50	1951—55
MEN															
0— 4	5.6	2.1	5.6	8.2	4.9	3.1	3.5	6.1	4.8	6.8	2.9	5.1	4.4	7.8	6.2
5— 9	0.8	1.6	3.0	3.6	4.4	1.7	3.0	2.3	3.7	4.7	0.8	3.1	2.4	3.8	3.6
10—14	2.1	3.0	3.3	4.5	3.1	1.1	2.2	3.0	3.9	3.2	1.5	0.8	1.5	3.1	2.4
15—19	2.0	1.3	2.9	1.6	2.2	1.1	2.2	3.9	3.5	3.8	1.9	2.0	1.2	2.9	3.4
20—24	1.7	1.0	3.8	1.7	2.5	1.1	0.6	2.0	1.6	2.3	1.1	1.9	2.7	2.0	2.8
25—29	2.2	2.4	2.6	4.8	2.5	1.8	2.2	3.1	5.3	1.5	1.5	1.6	1.0	2.2	2.8
30—34	1.2	3.7	2.0	2.1	2.4	—	1.7	3.0	2.5	1.9	1.9	1.8	2.5	3.6	1.7
35—39	0.7	1.2	2.8	3.1	1.8	1.4	2.5	5.4	2.9	4.1	1.5	2.6	3.5	2.0	3.1
40—44	—	4.7	5.0	3.4	2.8	—	4.8	1.8	3.8	3.9	3.2	3.4	2.6	3.2	5.5
45—49	4.3	6.8	4.0	6.4	4.8	5.2	3.1	4.1	5.6	9.3	4.1	5.1	4.3	4.4	3.0
50—54	6.7	6.2	9.6	6.3	6.1	4.9	4.4	5.6	8.4	5.7	10.8	6.6	5.7	9.2	7.7
55—59	16.0	16.4	9.4	9.3	9.8	10.4	11.1	14.5	12.4	19.4	8.1	7.9	14.0	10.8	8.2
60—64	13.5	20.3	14.9	22.9	19.0	11.5	22.2	25.8	23.7	8.8	10.3	14.9	11.1	10.3	18.0
65—69	26.8	23.2	24.5	28.0	36.4	20.4	17.6	21.1	19.8	29.3	12.4	15.2	17.1	27.9	34.6
70—74	17.6	29.7	36.4	43.6	43.7	12.5	18.0	22.4	26.2	32.7	16.1	15.8	29.8	32.1	27.5
75—79	19.5	40.9	44.0	39.3	74.4	11.1	32.1	27.3	44.7	70.8	10.1	16.7	14.9	16.3	32.0
80—84	10.5	27.3	43.5	23.1	52.9	7.4	6.1	24.2	10.8	26.1	2.9	5.8	—	7.1	21.8
85—	—	—	—	—	50.0	—	—	13.3	12.5	50.0	—	5.4	5.6	10.5	12.2
WOMEN															
0— 4	0.8	1.5	7.6	9.6	5.9	—	3.0	3.9	4.3	8.7	2.2	2.7	4.7	4.9	6.1
5— 9	2.3	0.8	1.5	0.6	1.5	1.7	2.4	1.2	1.9	2.8	1.0	2.2	3.2	2.5	2.9
10—14	0.7	—	0.8	3.0	2.5	0.5	0.5	1.8	1.7	1.9	1.0	0.9	1.1	3.2	3.2
15—19	0.6	1.6	1.3	2.9	2.0	1.5	1.9	1.0	2.5	2.8	1.2	2.5	1.4	1.6	3.1
20—24	1.4	—	1.8	1.0	1.8	1.4	—	0.4	2.6	1.8	1.0	1.5	0.6	1.5	0.6
25—29	0.5	0.4	3.1	0.9	—	1.5	2.4	2.3	1.3	1.8	1.9	1.9	1.5	1.4	1.6
30—34	1.0	0.4	2.2	3.2	4.4	2.2	1.5	1.4	2.8	1.3	2.9	2.0	1.9	1.7	1.6
35—39	2.8	2.0	0.9	3.6	2.0	3.1	2.8	3.6	3.3	1.4	2.1	1.8	2.0	2.4	1.9
40—44	1.3	3.9	2.0	2.9	3.3	1.4	1.3	2.8	1.0	4.2	2.1	3.8	2.4	4.0	3.5
45—49	1.4	7.0	6.3	2.6	4.5	—	1.4	5.0	3.9	6.1	5.2	4.1	1.6	5.7	6.2
50—54	2.3	4.3	9.3	5.8	7.0	4.5	3.2	5.1	3.8	9.4	5.6	3.1	4.2	9.0	6.6
55—59	8.2	7.2	10.3	8.2	7.3	3.1	8.3	10.5	7.4	11.3	6.7	7.0	7.6	4.5	8.8
60—64	9.1	14.6	12.9	9.3	14.7	7.5	15.3	8.6	8.3	11.3	8.4	6.4	7.2	10.3	10.6
65—69	9.8	20.3	18.3	18.9	24.0	9.1	13.5	23.0	11.1	21.8	5.9	13.4	12.8	12.5	19.6
70—74	10.9	20.3	24.2	11.5	22.3	5.9	16.4	7.9	17.6	14.0	3.8	11.2	7.2	18.3	22.5
75—79	—	10.3	35.7	25.5	30.5	—	11.0	14.8	28.0	14.3	1.5	10.0	5.5	17.1	18.8
80—84	5.9	18.2	17.8	12.0	63.2	—	—	9.3	8.2	24.6	—	—	—	7.0	8.2
85—	14.3	—	10.0	28.6	38.5	—	—	10.0	9.1	7.4	—	—	11.1	4.5	3.8

Table 37 a.

Cancerregisteret Denmark 1943–53
Number of Cases According to Year of Diagnosis.

	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953
Lymphogranulomatosis (Hodgkin), 201.											
MEN											
Capital	9	12	9	14	14	8	16	11	11	8	11
Provincial Towns	19	6	7	11	4	19	12	17	8	14	10
Rural Areas	23	24	21	24	22	28	31	21	27	25	34
Copenhagen Suburbs	1	3	0	0	2	5	2	1	1	4	1
WOMEN											
Capital	5	13	7	9	11	6	13	12	11	19	19
Provincial Towns	9	11	13	10	8	11	9	6	10	9	9
Rural Areas	23	10	10	17	11	16	17	18	16	13	11
Copenhagen Suburbs	1	1	1	1	1	1	2	2	1	6	3
MEN *Leukæmia, 204.0–204.4.*											
Capital											
Lymphatic leukæmia	16	17	16	19	16	21	16	17	25	21	15
Myeloid leukæmia	12	10	13	13	13	12	15	10	8	18	11
Other and unspecified leukæmia	5	2	4	3	5	5	7	11	9	6	5
Total	33	29	33	35	34	38	38	38	42	45	31
Provincial Towns											
Lymphatic leukæmia	20	26	26	22	26	22	25	29	16	33	35
Myeloid leukæmia	6	9	14	13	17	11	13	10	12	14	12
Other and unspecified leukæmia	6	4	6	3	5	4	2	1	3	6	9
Total	32	39	46	38	48	37	40	40	31	53	56
Rural Areas											
Lymphatic leukæmia	47	30	33	37	35	48	35	44	39	52	42
Myeloid leukæmia	19	18	25	14	20	21	18	25	15	24	23
Other and unspecified leukæmia	12	5	2	2	7	8	12	12	5	7	15
Total	78	53	60	53	62	77	65	81	59	83	80
Copenhagen Suburbs											
Lymphatic leukæmia	1	3	3	4	1	3	2	2	1	1	4
Myeloid leukæmia	0	1	1	3	2	2	2	2	5	5	4
Other and unspecified leukæmia	0	0	1	1	1	0	1	0	1	1	2
Total	1	4	5	8	4	5	5	4	7	7	10
WOMEN											
Capital											
Lymphatic leukæmia	16	12	14	5	7	20	19	15	16	17	16
Myeloid leukæmia	14	13	10	17	9	12	7	15	15	12	14
Other and unspecified leukæmia	4	8	2	2	4	8	11	3	6	10	4
Total	34	33	26	24	20	40	37	33	37	39	34
Provincial Towns											
Lymphatic leukæmia	14	12	13	11	14	9	12	13	14	20	11
Myeloid leukæmia	13	7	7	12	13	7	14	10	22	12	22
Other and unspecified leukæmia	3	2	5	4	4	8	8	0	9	4	6
Total	30	21	25	27	31	24	34	23	45	36	39
Rural Areas											
Lymphatic leukæmia	16	13	28	16	28	22	24	23	19	15	17
Myeloid leukæmia	17	14	16	20	15	17	28	8	29	14	18
Other and unspecified leukæmia	3	10	3	5	5	9	12	11	4	4	13
Total	36	37	47	41	48	48	64	42	52	33	48
Copenhagen Suburbs											
Lymphatic leukæmia	1	2	1	2	2	0	3	1	1	1	1
Myeloid leukæmia	2	2	3	3	2	0	0	3	2	1	0
Other and unspecified leukæmia	0	0	0	0	0	0	0	2	2	1	0
Total	3	4	4	5	4	0	3	6	5	3	1

Table 37 b.

Cancerregisteret Denmark 1943–53
Number of Cases According to Year of Diagnosis.

	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953
Multiple Myeloma, 203,											
MEN											
Capital	3	6	5	5	4	12	8	5	8	10	5
Provincial Towns	2	6	6	10	7	5	4	17	7	8	10
Rural Areas	10	15	14	12	8	17	12	10	12	18	16
Copenhagen Suburbs	1	1	1	0	0	1	1	0	2	0	1
WOMEN											
Capital	7	7	6	6	7	8	15	8	8	7	9
Provincial Towns	6	6	5	4	6	10	9	12	10	11	9
Rural Areas	5	7	10	7	10	5	7	10	10	11	11
Copenhagen Suburbs	0	0	3	0	1	1	0	3	0	2	1
Reticulo- and Lymphosarcoma, 200.0-200.1.											
MEN											
Capital	12	9	9	9	10	18	12	10	15	14	11
Provincial Towns	5	8	11	12	9	9	15	17	19	11	16
Rural Areas	19	19	14	11	12	18	20	13	22	20	22
Copenhagen Suburbs	0	0	0	0	4	3	2	3	3	3	1
WOMEN											
Capital	11	11	17	6	7	8	11	12	14	10	5
Provincial Towns	6	9	10	4	5	10	12	7	13	7	6
Rural Areas	10	6	13	14	6	13	10	17	17	15	6
Copenhagen Suburbs	0	2	2	0	3	2	1	0	2	1	1
Other and Unspecified Sarcoma, 200.2.											
MEN											
Capital	15	11	11	5	18	14	14	11	13	20	8
Provincial Towns	17	13	10	10	6	6	11	8	14	18	17
Rural Areas	13	21	23	15	24	20	17	12	22	19	24
Copenhagen Suburbs	3	3	1	1	1	1	2	4	2	1	0
WOMEN											
Capital	21	10	21	14	18	27	16	26	17	20	22
Provincial Towns	20	24	17	20	20	13	16	16	12	22	23
Rural Areas	33	22	26	27	29	20	30	21	23	29	26
Copenhagen Suburbs	1	1	0	1	3	3	4	5	4	1	1
Carcinoma and Sarcoma of Lymph System, 200.											
MEN											
Capital	6	1	4	3	3	6	3	3	6	1	3
Provincial Towns	3	3	6	3	4	5	3	3	5	8	3
Rural Areas	10	3	5	8	6	6	7	8	4	9	5
Copenhagen Suburbs	1	0	1	2	2	0	0	0	0	3	0
WOMEN											
Capital	4	2	3	0	6	1	4	2	1	3	5
Provincial Towns	5	1	4	3	3	3	0	1	2	7	3
Rural Areas	5	3	2	6	4	4	6	1	7	5	4
Copenhagen Suburbs	0	0	0	0	1	0	0	0	0	0	0
Malignant Neoplasms of Connective Tissue, 197.											
MEN											
Capital	7	4	3	9	10	13	16	7	15	12	11
Provincial Towns	9	11	9	12	13	14	14	15	22	11	9
Rural Areas	15	17	14	18	20	19	29	19	19	22	17
Copenhagen Suburbs	1	1	0	3	2	5	0	2	2	1	0
WOMEN											
Capital	5	3	4	9	6	12	15	7	9	13	10
Provincial Towns	10	15	11	10	6	12	11	16	11	17	20
Rural Areas	8	15	21	19	7	24	19	18	20	17	12
Copenhagen Suburbs	0	0	2	1	0	1	3	0	1	5	4

Table 38 a.

Cancerregisteret Denmark 1943–52.

Leukæmia. Number of Cases According to Sex, Age, and Habitation Area.

Period:	Capital		Provincial Towns		Rural Areas		Copenhagen Suburbs		Capital		Provincial Towns		Rural Areas		Copenhagen Suburbs	
	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52
Age	MEN				*Lymphatic Leukæmia, 204.0.*				WOMEN							
0— 4	7	4	11	9	20	22	1	—	5	9	8	9	16	17	1	—
5— 9	1	5	5	5	3	11	—	—	1	2	2	4	5	5	2	—
10—14	1	—	1	7	8	5	—	—	—	3	—	1	5	6	—	—
15—19	—	1	5	1	3	4	—	—	2	1	2	1	—	3	—	—
20—24	2	2	1	1	5	2	—	—	2	—	—	—	—	3	—	—
25—29	2	2	5	3	3	2	—	—	2	—	2	1	—	2	—	—
30—34	—	—	3	2	3	3	—	—	—	1	1	3	1	2	—	—
35—39	2	—	3	3	2	1	—	—	—	—	1	2	2	1	1	—
30—44	2	3	2	1	2	5	—	—	1	—	—	1	2	4	—	1
45—49	4	4	5	8	8	6	2	—	2	3	3	2	5	4	—	—
50—54	7	3	9	13	14	18	1	—	5	9	6	1	7	6	—	—
55—59	10	13	12	6	22	17	2	1	4	6	10	5	14	10	1	1
60—64	9	9	17	17	22	27	—	1	6	9	9	10	10	12	—	1
65—69	12	18	17	11	32	38	3	4	8	13	5	9	18	10	1	1
70—74	15	16	14	18	21	36	1	1	10	15	8	7	11	13	1	1
75—79	6	12	4	17	10	12	2	2	4	8	4	10	2	4	—	—
80—	2	8	5	3	4	9	—	—	1	8	2	2	3	1	1	1
Unknown	2	—	1	—	—	—	—	—	1	—	1	—	—	—	—	—
Total	84	100	120	125	182	218	12	9	54	87	64	68	101	103	8	6
					Myeloid Leukæmia, 204.1.											
0— 4	7	1	4	4	10	8	—	3	3	2	4	4	9	7	—	—
5— 9	2	2	2	2	4	2	—	—	—	—	2	1	3	5	2	—
10—14	2	6	1	1	7	1	—	1	2	1	1	3	2	6	—	—
15—19	—	1	1	3	6	7	—	—	1	—	1	2	2	2	1	—
20—24	4	—	5	1	3	7	—	—	—	—	2	2	2	2	—	—
25—29	4	4	5	3	4	3	—	3	1	2	1	1	4	—	—	—
30—34	6	2	3	5	6	6	—	2	1	1	1	1	5	3	—	—
35—39	3	2	4	—	9	6	1	—	5	6	4	3	6	8	1	—
40—44	1	3	4	2	3	9	—	1	3	4	1	5	6	10	4	—
45—49	4	7	1	6	10	4	—	2	8	3	6	8	12	12	2	—
50—54	2	—	4	7	6	9	2	1	5	5	4	6	5	13	1	1
55—59	2	6	9	3	9	8	1	—	7	5	7	7	7	10	—	—
60—64	6	6	6	8	8	8	—	1	12	4	4	6	6	6	—	1
65—69	7	7	5	5	6	10	2	2	6	12	4	7	4	3	1	2
70—74	7	9	2	4	5	11	1	—	3	8	7	3	3	6	—	1
75—79	4	5	2	3	—	4	—	—	5	4	2	6	4	3	—	1
80—	—	2	—	3	—	—	—	—	1	4	—	—	1	—	—	—
Unknown	—	—	1	—	—	—	—	—	—	—	1	—	1	—	—	—
Total	61	63	59	60	96	103	7	16	63	61	52	65	82	96	12	6
					Leukæmia, Other and Unspecified, 204.2 - 204.4.											
0— 4	2	9	2	1	5	3	—	—	2	5	3	9	3	8	—	1
5— 9	—	4	1	1	2	5	—	2	1	2	—	1	1	3	—	—
10—14	2	2	3	—	—	1	—	—	—	2	—	2	1	3	—	—
15—19	1	1	1	3	—	2	—	—	—	2	1	2	3	4	—	—
20—24	1	—	1	—	3	4	—	1	—	2	1	—	2	1	—	—
25—29	2	2	—	—	2	2	—	—	1	1	2	2	1	1	—	—
30—34	—	1	2	—	1	—	—	—	—	4	—	1	1	—	—	—
35—39	—	1	2	2	2	—	—	—	1	2	—	1	1	—	—	—
40—44	1	2	1	—	—	1	—	—	—	2	1	—	2	3	—	—
45—49	—	4	1	1	1	4	1	—	1	1	2	—	2	1	—	—
50—54	—	—	1	—	2	2	—	—	—	2	—	—	—	4	—	1
55—59	—	2	1	—	1	3	—	—	2	2	3	4	4	1	—	1
60—64	3	1	3	3	2	3	—	—	2	4	—	1	—	—	—	2
65—69	—	3	1	1	2	3	1	—	4	3	3	1	2	4	—	—
70—74	3	5	2	—	1	7	1	—	2	2	1	1	2	3	—	—
75—79	1	1	2	2	4	2	—	—	1	2	—	2	1	2	—	—
80—	1	—	—	2	—	2	—	—	2	—	1	2	—	2	—	—
Unknown	2	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—
Total	19	38	24	16	28	44	3	3	20	38	18	29	26	40	—	5

Table 38 b.

Cancerregisteret Denmark 1943–47 and 1948–52.
Lymphogranulomatosis and Sarcomas.
Number of Cases According to Sex, Age, and Habitation Area.

Period:	Capital 1943-47	Capital 1948-52	Provincial Towns 1943-47	Provincial Towns 1948-52	Rural Areas 1943-47	Rural Areas 1948-52	Copenhagen Suburbs 1943-47	Copenhagen Suburbs 1948-52	Capital 1943-47	Capital 1948-52	Provincial Towns 1943-47	Provincial Towns 1948-52	Rural Areas 1943-47	Rural Areas 1948-52	Copenhagen Suburbs 1943-47	Copenhagen Suburbs 1948-52
Age	MEN								WOMEN							
	Lymphogranulomatosis (Hodgkin), 201.															
0— 4	—	—	1	—	1	2	—	—	—	—	—	—	1	—	—	—
5— 9	—	2	—	—	3	1	—	1	—	1	—	—	—	2	—	—
10—14	1	—	—	—	2	3	—	—	—	—	2	—	1	2	—	—
15—19	3	2	4	5	6	9	—	—	2	5	1	1	6	5	1	1
20—24	4	4	7	14	8	13	—	2	1	4	5	3	11	10	1	—
25—29	9	3	4	9	12	20	1	3	11	5	10	10	8	11	1	2
30—34	7	5	3	5	18	12	1	2	7	9	8	4	11	5	—	3
35—39	10	7	7	4	9	13	1	—	5	5	4	4	5	5	1	1
40—44	6	10	2	3	10	11	1	1	1	3	4	2	7	10	—	2
45—49	3	1	3	6	8	6	1	2	3	4	6	5	3	5	1	—
50—54	1	2	3	8	4	9	1	—	2	8	1	4	1	2	—	—
55—59	5	3	3	6	11	7	—	—	2	7	4	4	4	6	—	—
60—64	4	4	2	5	9	9	—	—	4	2	1	4	4	6	—	—
65—69	1	8	4	2	6	7	—	1	2	3	5	—	3	4	—	1
70—74	3	2	—	2	3	8	—	1	2	2	—	2	2	3	—	2
75—79	1	—	1	1	4	2	—	—	2	—	—	1	1	2	—	—
80—	—	1	1	—	—	—	—	—	1	3	—	1	1	2	—	—
Unknown	—	—	2	—	—	—	—	—	—	—	—	—	2	—	—	—
Total	58	54	47	70	114	132	6	13	45	61	51	45	71	80	5	12
	Reticulo- and Lymphosarcoma, 200.0-200.1.															
0— 4	2	1	1	2	2	2	—	—	—	—	1	1	—	2	1	1
5— 9	—	1	2	1	—	—	—	—	—	—	—	1	—	1	—	—
10—14	—	1	—	—	—	5	—	—	2	—	1	1	—	—	—	—
15—19	—	1	1	1	1	—	—	2	—	—	—	1	2	3	—	—
20—24	3	1	—	—	1	2	—	—	—	2	—	—	—	—	—	—
25—29	1	3	1	2	4	2	—	—	—	—	2	—	1	1	1	—
30—34	3	3	1	2	3	2	1	1	1	2	1	1	1	—	1	1
35—39	5	2	4	3	5	5	—	1	3	3	3	1	4	4	—	1
40—44	2	1	3	5	5	3	—	—	4	2	2	5	1	3	—	—
45—49	5	5	6	7	7	7	—	1	3	3	4	5	4	4	1	1
50—54	6	10	5	12	4	9	—	2	5	—	1	1	6	5	—	—
55—59	4	5	4	7	9	5	—	4	4	8	3	7	1	7	1	—
60—64	3	12	7	11	7	11	1	—	12	3	5	7	6	11	—	1
65—69	3	8	6	8	13	12	—	1	6	8	3	1	5	9	1	—
70—74	6	10	1	1	7	13	2	1	6	8	4	8	7	8	—	—
75—79	3	2	2	5	5	9	—	1	2	9	3	5	6	9	1	1
80—	3	3	1	4	2	6	—	—	4	7	1	4	4	5	—	—
Unknown	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—
Total	49	69	45	71	75	93	4	14	52	55	34	49	49	72	7	6
	Other and Unspecified Sarcoma, 200.2.															
0— 4	—	1	7	2	4	6	2	1	2	3	2	2	4	3	—	—
5— 9	—	—	—	—	4	4	—	2	1	2	1	1	1	1	—	—
10—14	3	1	1	2	3	3	—	—	1	—	—	—	2	1	—	—
15—19	—	1	1	3	1	2	—	—	2	—	2	1	5	1	—	—
20—24	1	1	2	1	6	5	—	—	1	4	3	3	6	3	1	—
25—29	3	2	4	6	4	3	1	3	4	11	3	3	5	6	—	2
30—34	4	6	4	—	3	—	2	—	5	5	4	7	2	7	—	2
35—39	1	6	5	3	5	4	1	—	6	7	10	6	7	6	—	1
40—44	5	4	5	7	4	3	1	1	6	4	12	9	11	11	—	3
45—49	6	7	3	5	3	7	—	1	9	8	7	9	12	17	1	2
50—54	5	5	6	2	7	7	—	2	12	8	9	11	20	18	1	1
55—59	6	6	2	3	7	5	—	—	8	17	16	4	20	16	—	2
60—64	10	7	6	6	12	13	1	—	5	9	7	10	12	9	1	—
65—69	7	6	5	7	13	5	1	—	10	11	6	6	11	6	2	1
70—74	2	9	1	5	10	15	—	—	6	7	7	5	11	13	—	2
75—79	5	6	1	4	3	6	—	—	2	6	7	1	4	2	—	—
80—	2	4	3	1	7	2	—	—	4	4	3	1	2	3	—	1
Unknown	—	—	—	—	—	—	—	—	—	—	2	—	2	—	—	—
Total	60	72	56	57	96	90	9	10	84	106	101	79	137	123	6	17

Table 38 c.

Cancerregisteret Denmark 1943–47 and 1948–52.

Multiple Myeloma and Malignant Neoplasms of Lymph System and Connective Tissue.

Number of Cases According to Sex, Age, and Habitation Area.

Period:	Capital		Provincial Towns		Rural Areas		Copenhagen Suburbs		Capital		Provincial Towns		Rural Areas		Copenhagen Suburbs	
	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52
Age	MEN								WOMEN							
	Multiple Myeloma, 203.															
0— 4	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—
5— 9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	1	—	—	—	1	—	—	—	—	—	—
25—29	—	—	—	—	—	1	—	—	1	—	—	—	—	—	1	—
30—34	—	—	—	1	—	—	—	—	—	—	—	1	—	—	—	—
35—39	1	1	2	—	2	2	—	—	1	—	1	—	2	—	—	—
40—44	—	2	1	1	2	2	—	—	1	—	1	1	—	3	—	—
45—49	3	3	1	1	2	2	—	—	2	3	1	3	4	4	—	1
50—54	1	2	5	2	5	6	—	—	4	6	3	8	5	3	—	1
55—59	1	8	4	6	13	12	1	—	9	3	4	6	5	9	—	—
60—64	3	6	6	6	14	11	1	2	5	9	4	10	8	6	2	—
65—69	7	6	7	8	13	13	1	—	7	6	7	6	10	8	1	2
70—74	6	11	5	7	4	10	—	1	1	8	2	11	3	4	—	2
75—79	1	4	—	4	3	7	—	1	—	5	3	4	2	2	—	—
80—	—	—	—	4	—	1	—	—	1	5	1	2	—	4	—	—
Unknown	—	—	—	—	1	—	—	—	1	—	—	—	—	—	—	—
Total	23	43	31	41	59	69	3	4	33	46	27	52	39	43	4	6
	Carcinoma and Sarcoma of Lymph System, 202.															
0— 4	1	—	1	—	2	2	—	—	—	1	1	—	—	—	1	—
5— 9	1	2	—	—	—	—	—	—	—	—	1	—	—	—	—	—
10—14	—	1	—	—	—	—	—	1	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	1	—	—	—	—	—	—	1	—	—	—
20—24	—	1	2	—	1	—	—	—	1	—	—	—	1	1	—	—
25—29	—	—	1	—	—	3	—	—	—	1	1	—	2	2	—	—
30—34	1	1	—	1	2	—	—	—	—	—	1	1	—	—	—	—
35—39	—	1	3	5	1	1	2	—	1	2	2	1	—	—	—	—
40—44	—	2	—	1	—	7	—	—	—	—	—	—	—	1	—	—
45—49	4	2	2	4	3	1	—	—	1	—	1	1	—	2	—	—
50—54	3	1	1	3	5	3	2	1	4	—	—	1	—	3	—	—
55—59	1	1	2	2	2	4	—	—	2	1	—	—	3	4	—	—
60—64	1	3	3	—	4	6	—	—	3	2	1	1	6	5	—	—
65—69	1	1	3	1	3	4	1	—	—	1	2	4	2	—	—	—
70—74	2	2	1	5	4	1	—	—	—	—	5	—	3	3	—	—
75—79	1	1	—	1	2	—	1	—	2	1	—	3	—	—	—	—
80—	1	—	—	1	3	1	—	1	1	2	1	1	2	2	—	—
Unknown	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	17	19	19	24	32	34	6	3	15	11	16	13	20	23	1	—
	Malignant Neoplasms of Connective Tissue (not including skin), 197.															
0— 4	1	—	3	2	5	4	1	—	—	—	—	—	—	3	—	—
5— 9	1	2	—	—	2	2	—	1	—	2	1	1	—	1	—	—
10—14	—	—	2	1	3	3	1	—	—	2	2	1	5	2	—	1
15—19	1	1	1	—	5	5	—	—	—	1	3	2	1	1	—	—
20—24	—	1	5	1	4	5	—	—	—	1	2	6	2	3	—	—
25—29	2	2	1	6	1	3	—	—	—	2	3	2	1	5	—	1
30—34	—	3	1	1	3	2	—	2	1	3	2	6	—	6	—	2
35—39	3	3	1	6	1	8	—	—	2	—	1	1	6	2	—	—
40—44	3	5	3	9	5	9	2	2	1	4	5	9	5	11	—	—
45—49	5	7	3	7	6	8	—	2	3	3	3	6	5	12	—	3
50—54	3	7	6	8	7	11	—	—	2	8	7	5	4	6	—	—
55—59	3	6	7	3	6	10	2	—	5	6	3	7	8	14	1	1
60—64	7	10	6	12	7	5	—	1	5	7	3	4	9	12	—	1
65—69	2	6	4	7	9	12	1	1	2	4	6	6	10	7	1	1
70—74	1	3	8	4	7	6	—	—	1	5	6	4	9	4	1	—
75—79	—	3	2	8	8	2	—	1	4	3	2	3	4	5	—	—
80—	1	4	1	1	5	13	—	—	1	5	1	4	1	4	—	—
Unknown	—	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—
Total	33	63	54	76	84	108	7	10	27	56	52	67	70	98	3	10

Table 39.

Cancerregisteret Denmark 1943–52.
Cases of Lymphogranulomatosis (Hodgkin)
and Leukæmia Known from Death Certificates only.

Whole Country

Age	MEN								WOMEN							
	Lymphogranulomatosis (Hodgkin)		Lymphatic leukæmia		Myeloid leukæmia		Other and unspecified leukæmia		Lymphogranulomatosis (Hodgkin)		Lymphatic leukæmia		Myeloid leukæmia		Other and unspecified leukæmia	
	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52	1943-47	1948-52
0— 4	—	—	4	4	2	1	2	4	—	—	1	3	3	—	2	4
5— 9	—	—	1	1	—	—	—	2	—	—	—	—	1	—	—	1
10—14	—	—	—	1	—	—	1	—	—	—	—	1	—	1	—	1
15—19	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1
20—24	—	—	—	—	—	—	1	1	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	1	1	—	—	1	—	—	—	1	1
30—34	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
35—39	—	—	—	—	—	—	—	1	—	—	—	—	—	—	1	—
40—44	—	—	—	—	—	1	—	—	—	—	—	—	—	1	1	—
45—49	—	2	1	1	—	—	2	1	1	—	—	—	—	—	1	1
50—54	—	—	—	—	1	1	—	—	3	1	—	—	1	—	—	3
55—59	3	—	4	—	1	1	1	1	1	2	1	—	—	—	3	—
60—64	3	1	3	2	1	1	2	2	5	—	1	—	—	2	—	2
65—69	3	2	7	3	1	2	—	2	4	—	4	1	—	1	4	2
70—74	2	—	1	5	—	—	3	6	—	7	1	2	1	—	3	4
75—79	—	3	3	6	2	2	5	4	1	1	1	2	1	—	1	3
80—	—	2	1	5	—	1	1	1	—	3	1	2	—	—	1	3
Total	11	10	25	28	8	10	19	26	15	14	11	12	7	5	18	26
All cases	116	157	398	452	223	242	74	101	103	147	227	264	209	228	64	112
Capital																
Cases known from death certif. only	1	1	6	1	3	3	5	8	5	4	2	4	1	1	6	5
All cases	23	43	84	100	61	63	19	38	33	46	54	87	63	61	20	38
Provincial Towns																
Cases known from death certif. only	4	4	7	9	2	2	4	3	3	4	0	3	0	1	8	5
All cases	31	41	120	125	59	60	24	16	27	52	64	68	52	65	18	29
Rural Areas																
Cases known from death certif. only	6	5	11	17	1	5	9	13	6	5	9	5	6	3	4	14
All cases	59	69	182	218	96	103	28	44	39	43	101	103	82	96	26	40
Copenhagen Suburbs																
Cases known from death certif. only	0	0	1	1	2	0	1	2	1	1	0	0	0	0	0	2
All cases	3	4	12	9	7	16	3	3	4	6	8	6	12	6	0	5

Table 40.

Cases of Uncertain Diagnosis
(not included in other tables or figures)

Whole country																
	27	18	3	3	5	2	5	11	20	15	3	4	1	5	6	8
Capital																
	6	3	1	0	1	0	0	3	5	3	3	1	1	1	1	2
Provincial Towns																
	9	9	2	0	1	1	3	4	7	5	0	0	0	0	1	1
Rural Areas																
	11	6	0	3	3	1	2	4	8	7	0	3	0	4	4	5
Copenhagen Suburbs																
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 41 a.

Cancerregisteret Denmark 1943–52.

Verification of Diagnosis.

		All cases	Admitted in hospital number	Admitted in hospital per cent	Histologically verified number	Histologically verified per cent of all cases	Histologically verified per cent of hosp. cases	Number of deaths	Autopsies number	Autopsies per cent of all cases	Autopsies per cent of deaths	Malignancy diagnosis before death unstated number	Malignancy diagnosis before death per cent certain	Malignancy diagnosis before death per cent suspected	Malignancy diagnosis before death per cent unknown	Grading of validity of diagnosis per cent of all cases 1°	2°	3°
MEN																		
								Lymphogranulomatosis (Hodgkin), 201.										
Capital	1943—47	58	52	90	41	71	79	47	27	47	57	4	78	17	4	76	0	24
	1948—52	54	52	96	43	80	83	44	28	52	64	1	74	7	19	87	4	9
Provincial	1943—47	47	44	94	30	64	68	41	10	21	24	3	86	14	0	68	2	30
Towns	1948—52	70	64	91	44	63	69	55	21	30	38	7	86	14	0	66	0	34
Rural Areas	1943—47	114	101	89	79	69	78	103	25	22	24	7	56	33	11	72	0	28
	1948—52	132	114	86	75	57	66	99	27	20	27	3	79	8	13	62	1	37
Copenhagen	1943—47	6	6	100	6	100	100	6	4	67	67	2	100	0	0	100	0	0
Suburbs	1948—52	13	12	92	10	77	83	11	6	46	55	0	83	17	0	77	0	23
WOMEN																		
Capital	1943—47	45	39	87	29	64	74	33	14	31	42	0	50	14	36	69	0	31
	1948—52	61	53	87	40	66	75	44	21	34	48	3	67	22	11	70	0	30
Provincial	1943—47	51	48	94	34	67	71	35	6	12	17	1	100	0	0	69	2	29
Towns	1948—52	45	42	93	28	62	67	26	7	16	27	4	67	33	0	64	0	36
Rural Areas	1943—47	71	62	87	42	59	68	55	7	10	13	5	100	0	0	61	1	38
	1948—52	80	73	91	46	58	63	58	10	12	17	2	88	12	0	59	1	40
Copenhagen	1943—47	5	5	100	5	100	100	3	1	20	33	0	100	0	0	100	0	0
Suburbs	1948—52	12	11	92	9	75	82	5	1	8	20	1	—	—	—	75	0	25
MEN																		
								Lymphatic Leukæmia, 204.0.										
Capital	1943—47	84	76	90	39	46	51	81	52	62	64	16	75	6	19	68	8	24
	1948—52	100	99	99	64	64	65	87	50	50	57	9	71	15	15	73	8	19
Provincial	1943—47	120	113	94	44	37	39	114	32	27	28	12	90	0	10	49	24	27
Towns	1948—52	125	116	93	49	39	42	109	26	21	24	4	95	0	5	46	18	36
Rural Areas	1943—47	182	171	94	60	33	35	169	34	19	20	17	82	18	0	41	30	29
	1948—52	218	200	92	91	42	46	195	41	19	21	12	90	3	7	46	17	37
Copenhagen	1943—47	12	11	92	5	42	45	11	7	58	64	4	33	33	33	67	17	17
Suburbs	1948—52	9	8	89	8	89	100	8	6	67	75	2	100	0	0	89	0	11
WOMEN																		
Capital	1943—47	54	51	94	27	50	53	50	25	46	50	6	68	21	11	59	20	20
	1948—52	87	82	94	52	60	63	72	35	40	49	2	82	9	9	64	14	22
Provincial	1943—47	64	63	98	21	33	33	60	14	22	23	4	80	10	10	41	33	27
Towns	1948—52	68	64	94	38	56	59	59	21	31	36	4	88	12	0	66	15	19
Rural Areas	1943—47	101	92	91	30	30	33	91	13	13	14	5	100	0	0	37	24	40
	1948—52	103	98	95	40	39	41	84	19	18	23	7	92	0	8	41	35	24
Copenhagen	1943—47	8	8	100	3	38	38	8	4	50	50	2	50	0	50	50	13	38
Suburbs	1948—52	6	6	100	4	67	67	5	3	50	60	0	100	0	0	67	17	17

								Myeloid Leukæmia, 204.1.										
MEN																		
Capital	1943—47	61	56	92	38	62	68	61	37	61	61	10	63	19	19	77	3	20
	1948—52	63	60	95	37	59	62	57	38	60	67	5	73	15	12	76	5	19
Provincial	1943—47	59	56	95	20	34	36	55	10	17	18	6	75	25	0	39	32	29
Towns	1948—52	60	58	97	29	48	50	58	24	40	41	5	95	5	0	60	12	28
Rural Areas	1943—47	96	95	99	36	38	38	96	26	27	27	12	93	7	0	50	33	17
	1948—52	103	97	94	36	35	37	95	23	22	24	6	94	6	0	44	23	33
Copenhagen	1943—47	7	5	71	2	29	29	7	3	43	43	1	50	50	0	43	14	43
Suburbs	1948—52	16	16	100	11	69	69	16	10	62	62	0	90	0	10	75	19	6
WOMEN																		
Capital	1943—47	63	59	94	38	60	64	61	37	59	61	12	72	12	16	78	8	14
	1948—52	61	60	98	45	74	75	58	42	69	72	8	82	9	9	82	8	10
Provincial	1943—47	52	52	100	17	33	33	52	15	29	29	4	91	9	0	48	33	19
Towns	1948—52	65	64	98	32	49	50	61	19	29	31	4	87	0	13	52	28	20
Rural Areas	1943—47	82	75	91	28	34	37	80	19	23	24	13	100	0	0	45	24	30
	1948—52	96	92	96	40	42	43	83	29	30	35	6	87	13	0	50	19	31
Copenhagen	1943—47	12	12	100	7	58	58	12	5	42	42	2	100	0	0	67	33	0
Suburbs	1948—52	6	6	100	4	67	67	5	4	67	80	0	100	0	0	67	15	16
								Leukæmia, Other and Unspecified, 204.2 - 204.4.										
MEN																		
Capital	1943—47	19	12	63	8	42	67	18	7	37	39	2	40	20	40	53	5	42
	1948—52	38	30	79	19	38	63	38	22	58	58	5	82	12	6	63	3	34
Provincial	1943—47	24	19	79	7	29	37	24	9	38	38	5	75	25	0	46	21	33
Towns	1948—52	16	12	75	4	25	33	16	4	25	25	0	100	0	0	44	31	25
Rural Areas	1943—47	28	18	64	4	14	22	28	1	4	4	0	100	0	0	14	25	61
	1948—52	44	31	70	9	20	29	44	6	14	14	3	67	33	0	30	23	48
Copenhagen	1943—47	3	2	67	1	33	50	3	2	67	67	2	—	—	—	67	0	33
Suburbs	1948—52	3	1	33	0	—	—	3	1	14	33	0	100	0	0	33	0	67
WOMEN																		
Capital	1943—47	20	8	40	5	25	62	20	4	20	20	3	100	0	0	30	5	65
	1948—52	38	33	87	17	45	52	38	20	53	53	3	100	0	0	66	11	24
Provincial	1943—47	18	9	50	8	44	89	18	2	11	11	1	0	100	0	44	6	50
Towns	1948—52	29	24	83	4	14	17	28	3	10	11	0	67	0	33	21	28	52
Rural Areas	1943—47	26	19	73	4	15	21	25	5	19	20	3	50	50	0	27	27	46
	1948—52	40	25	62	10	25	40	38	5	32	13	1	50	50	0	32	20	48
Copenhagen	1943—47	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Suburbs	1948—52	5	3	60	0	—	—	4	0	—	—	0	—	—	—	0	40	60
								Multiple Myeloma, 203.										
MEN																		
Capital	1943—47	23	22	96	11	48	50	23	15	65	65	2	77	15	8	70	9	22
	1948—52	43	42	98	25	58	60	39	22	51	56	3	79	11	11	74	16	9
Provincial	1943—47	31	26	84	15	48	58	30	10	32	33	4	100	0	0	55	26	19
Towns	1948—52	41	36	88	19	46	53	38	13	32	34	4	56	22	22	51	17	32
Rural Areas	1943—47	59	52	88	16	27	31	58	19	32	33	9	50	40	10	42	37	20
	1948—52	69	64	93	29	42	45	59	13	19	22	4	89	0	11	48	29	23
Copenhagen	1943—47	3	3	100	3	100	100	3	3	100	100	1	50	50	0	100	0	0
Suburbs	1948—52	4	4	100	3	75	75	4	3	75	75	2	100	0	0	75	25	0

Table 41 b.

Cancerregisteret Denmark 1943–52.

Verification of Diagnosis.

		All cases	Admitted in hospital number	Admitted in hospital per cent	Histologically verified number	Histologically verified per cent of all cases	Histologically verified per cent of hosp. cases	Number of deaths	Autopsies number	Autopsies per cent of all cases	Autopsies per cent of deaths	Malignancy diagnosis before death unstated number	Malignancy diagnosis before death per cent certain	Malignancy diagnosis before death per cent suspected	Malignancy diagnosis before death per cent unknown	Grading of validity of diagnosis per cent of all cases 1°	2°	3°
WOMEN																		
								Multiple Myeloma, 203. (continued)										
Capital	1943—47	33	27	82	14	42	52	33	16	48	48	1	73	13	13	55	9	36
	1948—52	46	41	89	22	48	54	39	22	48	56	2	75	10	15	54	15	30
Provincial	1943—47	27	24	89	7	26	29	26	5	19	19	2	100	0	0	30	37	33
Towns	1948—52	52	48	92	21	40	44	48	9	17	19	2	86	0	14	55	29	40
Rural Areas	1943—47	39	33	85	14	36	42	36	6	15	17	5	100	0	0	44	28	28
	1948—52	43	38	88	19	44	50	38	4	9	11	2	100	0	0	49	21	30
Copenhagen	1943—47	4	3	75	2	50	67	4	1	25	25	0	0	100	0	50	25	25
Suburbs	1948—52	6	5	83	3	50	60	6	2	33	33	0	100	0	0	50	17	33
MEN																		
								Reticulo- and Lymphosarcoma, 200.0 - 200.1.										
Capital	1943—47	49	48	98	39	80	81	40	27	55	68	2	52	32	16	88	0	12
	1948—52	69	67	97	60	87	90	60	39	57	65	3	58	25	17	88	1	10
Provincial	1943—47	45	45	100	38	84	84	36	10	22	28	6	50	25	25	89	0	11
Towns	1948—52	71	69	97	62	87	90	57	18	25	32	7	64	27	9	89	1	10
Rural Areas	1943—47	75	75	100	68	91	91	64	23	31	36	12	55	27	18	92	0	8
	1948—52	93	89	96	76	82	85	78	22	24	28	6	69	25	6	83	1	16
Copenhagen	1943—47	4	4	100	4	100	100	3	2	50	67	2	—	—	—	100	0	0
Suburbs	1948—52	14	14	100	13	93	93	12	7	50	58	2	60	20	20	100	0	0
WOMEN																		
Capital	1943—47	52	51	98	44	85	86	42	24	46	57	3	52	33	14	90	0	10
	1948—52	55	55	100	53	96	96	45	27	49	60	2	64	28	8	96	2	2
Provincial	1943—47	34	34	100	33	97	97	27	12	35	44	4	75	12	12	97	0	3
Towns	1948—52	49	49	100	40	82	82	37	11	22	30	2	89	11	0	88	2	10
Rural Areas	1943—47	49	48	98	41	84	85	41	10	20	24	3	86	14	0	86	0	14
	1948—52	72	71	99	63	88	89	53	13	18	25	5	75	12	12	88	0	13
Copenhagen	1943—47	7	7	100	6	86	86	6	2	29	33	1	100	0	0	86	0	14
Suburbs	1948—52	6	5	83	4	67	80	5	2	33	40	0	0	100	0	67	0	33
MEN																		
								Other and Unspecified Sarcoma, 200.2										
Capital	1943—47	60	57	95	46	77	81	49	36	60	73	11	40	36	24	87	0	13
	1948—52	72	70	97	67	93	96	51	41	57	80	3	58	29	13	94	0	6
Provincial	1943—47	56	55	98	44	79	80	43	12	21	28	4	75	25	0	80	0	20
Towns	1948—52	57	52	91	48	84	92	35	9	16	26	0	33	33	33	84	0	16
Rural Areas	1943—47	96	83	86	64	67	77	78	14	15	18	9	100	0	0	69	0	31
	1948—52	90	86	96	77	86	90	55	14	16	25	4	56	22	22	87	0	13
Copenhagen	1943—47	9	7	78	6	67	86	8	5	56	62	3	100	0	0	78	0	22
Suburbs	1948—52	10	10	100	9	90	90	8	6	60	75	0	67	0	33	90	0	10

WOMEN																		
Capital	1943—47	84	80	95	71	85	89	53	28	33	53	4	71	21	8	88	0	12
	1948—52	106	106	100	102	96	96	54	31	29	57	3	50	18	32	97	0	3
Provincial	1943—47	101	95	94	83	82	87	73	18	18	25	9	78	22	0	84	0	16
Towns	1948—52	79	77	97	71	90	92	35	7	9	20	1	67	33	0	91	0	9
Rural Areas	1943—47	137	122	89	102	74	84	96	16	12	17	9	86	14	0	77	0	23
	1948—52	123	116	94	105	85	91	56	10	8	18	1	78	11	11	85	0	15
Copenhagen	1943—47	6	6	100	4	67	67	2	0	—	—	—	—	—	—	67	0	33
Suburbs	1948—52	17	17	100	15	88	88	8	2	12	25	—	—	—	—	88	0	12
								Carcinoma and Sarcoma of Lymph System, 202.										
Capital	1943—47	17	17	100	14	82	82	17	12	71	71	1	27	64	9	94	0	6
	1948—52	19	19	100	17	89	89	19	16	84	84	1	53	33	13	100	0	0
Provincial	1943—47	19	16	84	14	74	88	19	8	42	42	3	60	40	0	79	0	21
Towns	1948—52	24	23	96	20	83	87	21	11	46	52	3	88	12	0	88	0	13
Rural Areas	1943—47	32	27	84	25	78	93	31	12	38	39	5	57	43	0	81	3	16
	1948—52	34	33	97	27	79	82	29	8	24	28	3	60	40	0	82	0	18
Copenhagen	1943—47	6	6	100	4	67	67	4	2	33	50	1	0	100	0	67	0	33
Suburbs	1948—52	3	3	100	2	67	67	2	1	33	50	0	0	0	100	67	0	33
WOMEN																		
Capital	1943—47	15	13	87	11	73	85	15	10	67	67	2	63	25	12	80	0	20
	1948—52	11	11	100	9	82	82	7	7	64	100	1	83	17	0	82	9	9
Provincial	1943—47	16	16	100	15	94	94	13	5	31	38	2	33	0	67	94	0	6
Towns	1948—52	13	13	100	11	85	85	12	7	54	58	4	67	33	0	92	0	8
Rural Areas	1943—47	20	18	90	15	75	83	19	4	20	21	3	100	0	0	80	0	20
	1948—52	23	21	91	18	78	86	20	8	35	40	3	80	20	0	87	0	13
Copenhagen	1943—47	1	1	100	1	100	100	1	1	100	100	0	0	100	0	100	0	0
Suburbs	1948—52	0	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
MEN								*Malignant Neoplasms of Connective Tissue, 197.*										
Capital	1943—47	33	30	91	26	79	87	22	8	24	36	2	83	17	0	79	0	21
	1948—52	63	62	98	54	86	87	34	15	24	44	1	86	14	0	86	1	13
Provincial	1943—47	54	49	91	42	78	86	40	9	16	23	5	75	25	0	78	0	22
Towns	1948—52	76	73	96	64	84	88	42	9	12	21	1	100	0	0	84	0	16
Rural Areas	1943—47	84	77	92	67	80	87	52	4	5	8	2	100	0	0	80	1	19
	1948—52	108	102	94	78	72	76	73	11	10	15	3	75	25	0	72	0	28
Copenhagen	1943—47	7	6	86	6	86	100	5	2	29	40	1	100	0	0	86	0	14
Suburbs	1948—52	10	10	100	7	70	70	4	0	—	—	0	—	—	—	70	10	20
WOMEN																		
Capital	1943—47	27	25	93	24	89	96	13	6	22	46	1	40	60	0	89	0	11
	1948—52	56	52	93	44	79	85	27	12	21	44	0	75	17	8	80	0	20
Provincial	1943—47	52	50	96	44	85	88	29	2	4	7	0	100	0	0	85	0	15
Towns	1948—52	67	63	94	60	90	95	28	6	9	21	1	80	20	0	90	0	10
Rural Areas	1943—47	70	65	93	61	87	94	40	1	1	2	0	100	0	0	87	1	12
	1948—52	98	93	95	81	83	87	46	5	5	11	2	100	0	0	83	0	17
Copenhagen	1943—47	3	3	100	3	100	100	3	1	33	33	1	—	—	—	100	0	0
Suburbs	1948—52	10	10	100	9	90	90	5	1	10	20	1	—	—	—	90	0	10

Table 42.
Cancerregisteret Denmark 1943–52.
Acute and Chronic Leukæmia.

Age	Acute leukæmia								Chronic leukæmia							
	Absolute numbers				Rates per million				Absolute numbers				Rates per million			
	Lymphatic	Myeloid	Others	All	Lymphatic	Myeloid	Others	All	Lymphatic	Myeloid	Others	All	Lymphatic	Myeloid	Others	All
MEN																
0— 4	35	24	12	71	16.9	11.6	5.8	34.3	39	13	10	62	18.8	6.3	4.8	29.9
5— 9	13	9	9	31	7.3	5.0	5.0	17.3	17	5	6	28	9.5	2.8	3.4	15.7
10—14	7	13	4	24	4.5	8.4	2.6	15.5	15	6	4	25	9.7	3.9	2.6	16.1
15—19	7	10	5	22	4.6	6.6	3.3	14.5	7	8	3	18	4.6	5.3	2.0	11.9
20—24	6	7	2	15	3.9	4.5	1.3	9.7	7	13	8	28	4.5	8.4	5.1	18.0
25—29	8	13	1	22	5.1	8.3	0.6	14.0	9	12	7	29	5.7	7.6	4.5	18.5
30—34	6	13	1	20	3.8	8.3	0.6	12.7	5	17	3	25	3.2	10.8	1.9	15.9
35—39	3	2	—	5	1.9	1.3	—	3.2	8	23	7	38	5.1	14.8	4.5	24.4
40—44	3	6	2	11	2.1	4.1	1.4	7.6	12	17	3	32	8.3	11.7	2.1	22.1
45—49	2	6	3	11	1.5	4.6	2.3	8.5	35	28	9	72	26.9	21.5	6.9	55.4
50—54	7	3	1	11	6.1	2.6	0.9	9.7	58	28	4	90	50.9	24.6	3.5	79.0
55—59	2	7	3	12	2.0	7.1	3.0	12.2	81	31	4	116	82.3	31.5	4.1	117.9
60—64	5	4	1	10	6.0	4.8	1.2	11.9	97	39	14	150	115.6	46.5	16.7	178.8
65—69	9	5	4	18	13.1	7.3	5.8	26.2	126	39	7	172	183.4	56.8	10.2	250.4
70—74	1	7	3	11	2.0	14.0	6.0	22.0	121	32	16	169	242.3	64.1	32.0	338.4
75—79	3	2	1	6	9.8	6.5	3.3	19.6	62	16	11	89	202.7	52.3	36.0	291.0
80—	2	1	1	4	9.4	4.7	4.7	18.7	29	4	4	37	135.6	18.7	18.7	173.0
Total	119	132	53	304					728	332	120	1180				
WOMEN																
0— 4	29	14	16	59	14.7	7.1	8.1	29.9	36	15	15	66	18.2	7.6	7.6	33.4
5— 9	9	4	2	15	5.2	2.3	1.2	8.7	12	9	6	27	7.0	5.2	3.5	15.7
10—14	5	6	5	16	3.0	4.0	3.0	10.6	10	9	3	22	6.6	6.0	2.0	14.6
15—19	3	4	7	14	2.0	2.7	4.7	9.5	6	5	5	16	4.1	3.4	3.4	10.8
20—24	3	4	1	8	1.9	2.6	0.6	5.2	2	4	5	11	1.3	2.6	3.2	7.1
25—29	—	2	2	4	—	1.3	1.3	2.5	7	7	6	20	4.4	4.4	3.8	12.5
30—34	4	6	3	13	2.5	3.8	1.9	8.1	4	6	3	13	2.5	3.8	1.9	8.1
35—39	4	7	1	12	2.5	4.4	0.6	7.6	3	26	4	33	1.9	16.4	2.5	20.9
40—44	1	8	2	11	0.7	5.4	1.3	7.4	8	25	6	39	5.4	16.7	4.0	26.1
45—49	1	14	1	16	0.7	10.2	0.7	11.7	18	37	6	61	13.1	27.0	4.4	44.5
50—54	4	9	2	15	3.3	7.4	1.6	12.3	30	31	5	66	24.6	25.4	4.1	54.2
55—59	2	7	3	12	1.9	6.6	2.8	11.3	49	36	14	99	46.2	33.9	13.2	93.3
60—64	3	5	5	13	3.3	5.5	5.5	14.3	54	34	4	92	59.3	37.3	4.4	101.0
65—69	5	5	1	11	6.7	6.7	1.3	14.8	60	34	16	110	80.6	45.7	21.5	147.8
70—74	4	6	—	10	7.3	11.0	—	18.3	62	25	11	98	113.7	45.8	20.2	179.7
75—79	1	7	1	9	2.9	20.1	2.9	25.8	31	18	7	56	88.9	51.6	20.1	160.6
80—	1	—	1	2	3.7	—	3.7	7.4	18	6	7	31	66.4	22.1	25.8	114.4
Total	79	108	53	240					410	327	123	860				

Total	79	108	53	240		410	327	123	860	

Table 43 a.

Cancerregisteret Denmark 1943–52.

Leukæmia. Incidence Rates per 10,000.

Age	LYMPHATIC LEUKÆMIA, 204.0.					MYELOID LEUKÆMIA, 204.1.					ALL LEUKÆMIA, 204.0 - 204.4.				
	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark
MEN															
0— 4	.27	.36	.42	.10	.36	.20	.15	.18	.29	.18	.74	.56	.67	.39	.64
5— 9	.18	.23	.15	—	.17	.12	.09	.06	—	.08	.42	.36	.29	.23	.33
10—14	.04	.22	.15	—	.14	.30	.06	.09	.16	.12	.49	.36	.25	.16	.32
15—19	.04	.17	.08	—	.09	.04	.11	.15	—	.12	.16	.40	.26	—	.26
20—24	.12	.05	.09	—	.08	.12	.16	.13	—	.13	.26	.24	.31	.15	.28
25—29	.11	.20	.07	—	.11	.22	.20	.10	.36	.17	.44	.39	.22	.36	.32
30—34	—	.12	.08	—	.07	.21	.20	.17	.25	.19	.24	.37	.27	.25	.29
35—39	.05	.15	.04	—	.07	.13	.10	.21	.14	.16	.21	.35	.28	.14	.28
40—44	.14	.08	.10	—	.10	.12	.17	.18	.16	.16	.35	.28	.30	.16	.30
45—49	.26	.40	.23	.37	.28	.35	.22	.23	.37	.26	.74	.68	.54	.93	.64
50—54	.36	.78	.60	.23	.57	.07	.39	.28	.68	.27	.43	1.20	.95	.90	.89
55—59	.98	.74	.83	.85	.84	.34	.50	.36	.28	.39	1.41	1.28	1.27	1.13	1.30
60—64	.95	1.64	1.18	.36	1.22	.63	.67	.39	.36	.51	1.79	2.60	1.69	.72	1.91
65—69	1.99	1.62	2.04	3.30	1.97	.93	.58	.47	1.88	.64	3.12	2.32	2.66	5.65	2.77
70—74	2.94	2.55	2.25	1.34	2.44	1.52	.48	.63	.67	.78	5.21	3.19	3.20	2.68	3.60
75—79	3.01	2.73	1.36	5.18	2.13	1.50	.65	.25	—	.59	4.84	3.90	1.98	5.18	3.11
80—	2.77	1.51	1.08	—	1.45	.55	.57	—	—	.23	3.60	2.45	1.24	—	1.92
WOMEN															
0— 4	.36	.32	.34	.10	.33	.13	.15	.17	—	.15	.67	.70	.62	.20	.63
5— 9	.09	.14	.11	.25	.12	—	.07	.09	.25	.08	.18	.23	.25	.49	.24
10—14	.11	.08	.13	—	.10	.11	.11	.10	—	.10	.30	.19	.28	—	.25
15—19	.11	.07	.04	—	.06	.04	.07	.05	.17	.06	.21	.22	.19	.17	.20
20—24	.05	.04	.05	—	.03	—	.09	.06	—	.05	.10	.11	.16	—	.12
25—29	.05	.04	.03	—	.04	.07	.04	.06	—	.06	.16	.20	.13	—	.15
30—34	.02	.02	.05	—	.05	.05	.05	.12	—	.08	.16	.16	.19	—	.16
35—39	—	—	.05	.13	.04	.25	.17	.21	.13	.21	.32	.27	.27	.27	.28
40—44	.02	.03	.10	.15	.06	.17	.15	.25	.62	.22	.24	.21	.43	.77	.33
45—49	.13	.14	.16	—	.14	.29	.39	.41	.37	.37	.48	.59	.62	.37	.56
50—54	.42	.45	.25	—	.28	.30	.32	.34	.44	.33	.77	.54	.67	.67	.66
55—59	.34	.37	.52	.56	.48	.41	.51	.37	—	.41	.89	1.32	1.00	.83	1.05
60—64	.59	.63	.56	.35	.63	.63	.42	.31	.35	.43	1.46	1.26	.87	1.42	1.15
65—69	1.00	1.07	.89	.91	.87	.86	.56	.22	1.36	.52	2.20	1.47	1.30	2.27	1.63
70—74	1.64	1.71	1.04	1.34	1.21	.72	.69	.39	.67	.57	2.62	1.85	1.64	2.01	1.98
75—79	1.26	1.28	.40	—	.92	.95	.85	.46	1.14	.72	2.53	2.56	1.06	1.14	1.86
80—	1.25	1.26	.33	3.19	.70	.70	—	.08	—	.22	2.23	.98	.58	3.19	1.18

Table 43 b.

Cancerregisteret Denmark 1943–52.

Lymphogranulomatosis and Sarcoma. Incidence Rates per 10,000.

Age	LYMPHOGRANULOMATOSIS (HODGKIN), 201.					RETICULO- AND LYMPHOSARCOMA, 200.0-200.1.					OTHER AND UNSPECIFIED SARCOMA, 200.2.				
	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark	Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark
MEN															
0— 4	—	.02	.03	—	.02	.07	.05	.04	—	.05	.02	.16	.10	.29	.11
5— 9	.06	—	.04	.12	.04	.03	.07	—	—	.02	—	—	.09	.23	.06
10—14	.04	—	.06	—	.04	.04	—	.06	—	.04	.15	.08	.07	—	.08
15—19	.20	.26	.17	—	.19	.04	.06	.01	.37	.04	.04	.11	.03	—	.05
20—24	.23	.56	.27	.30	.33	.12	—	.04	—	.05	.06	.08	.14	—	.10
25—29	.33	.32	.45	.48	.39	.11	.07	.08	—	.08	.14	.25	.10	.48	.17
30—34	.32	.20	.42	.37	.34	.16	.07	.07	.25	.10	.27	.10	.04	.25	.12
35—39	.46	.28	.31	.14	.33	.19	.18	.14	.14	.16	.19	.20	.13	.14	.16
40—44	.46	.14	.31	.31	.30	.09	.22	.12	—	.13	.26	.33	.10	.31	.21
45—49	.13	.28	.23	.56	.23	.32	.40	.23	.19	.29	.42	.25	.16	.19	.25
50—54	.11	.39	.24	.23	.25	.58	.60	.24	.45	.42	.36	.28	.26	.45	.30
55—59	.34	.37	.38	—	.36	.38	.45	.30	1.13	.39	.51	.21	.25	—	.29
60—64	.42	.34	.43	—	.39	.79	.87	.43	.36	.62	.90	.58	.60	.36	.66
65—69	.60	.35	.38	.47	.42	.73	.81	.73	.47	.74	.86	.70	.53	.47	.64
70—74	.47	.16	.43	.67	.38	1.52	.16	.79	2.01	.82	1.04	.48	.99	—	.84
75—79	.17	.26	.37	—	.29	.83	.91	.87	1.30	.85	1.84	.65	.56	—	.82
80—	.28	.19	—	—	.09	1.66	.94	.66	—	.89	1.66	.75	.75	—	.94
WOMEN															
0— 4	—	—	.01	—	.01	—	.04	.02	.20	.03	.13	.08	.07	—	.08
5— 9	.03	—	.02	—	.02	—	.02	.01	—	.01	.09	.05	.02	—	.04
10—14	—	.06	.04	—	.03	.08	.06	—	—	.03	.04	—	.04	—	.03
15—19	.25	.05	.15	.34	.15	—	.02	.07	—	.04	.07	.07	.08	—	.07
20—24	.13	.17	.34	.13	.23	.05	—	—	—	.01	.13	.13	.15	.13	.14
25—29	.37	.44	.30	.34	.36	—	.04	.03	.11	.03	.35	.13	.18	.23	.21
30—34	.37	.28	.25	.37	.29	.07	.05	.02	.24	.05	.23	.25	.14	.24	.20
35—39	.23	.19	.15	.27	.19	.14	.10	.12	.13	.12	.30	.39	.20	.13	.27
40—44	.10	.15	.27	.31	.19	.15	.18	.06	—	.11	.24	.54	.35	.46	.37
45—49	.18	.31	.14	.19	.20	.16	.25	.14	.37	.18	.45	.45	.50	.56	.47
50—54	.30	.16	.06	—	.15	.15	.06	.21	—	.15	.59	.64	.73	.44	.66
55—59	.31	.29	.22	—	.25	.41	.37	.17	.28	.29	.86	.73	.78	.56	.78
60—64	.24	.21	.26	—	.23	.59	.50	.43	.35	.49	.55	.71	.54	.35	.58
65—69	.24	.25	.22	.45	.24	.67	.20	.44	.45	.44	1.00	.61	.54	1.36	.71
70—74	.26	.14	.22	1.34	.24	.92	.82	.65	—	.75	.85	.82	1.04	1.34	.94
75—79	.21	.11	.20	—	.17	1.16	.85	.99	2.28	1.03	.84	.85	.40	—	.63
80—	.56	.14	.25	—	.30	1.53	.70	.74	—	.92	1.11	.56	.41	1.60	.66

Table 43 c. *Cancerregisteret Denmark 1943–52. Incidence Rates per 10.000.*

Age	MULTIPLE MYELOMA, 203. Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark	MALIGNANT NEOPLASMS OF CONNECTIVE TISSUE, 197. Capital	Provincial Towns	Rural Areas	Copenhagen Suburbs	Denmark
MEN										
0— 4	—	—	.01	—	.00	.02	.09	.09	.10	.08
5— 9	—	—	—	—	—	.09	—	.04	.12	.04
10—14	—	.03	—	—	.01	—	.08	.07	.16	.06
15—19	—	—	—	—	—	.08	.03	.12	—	.09
20—24	—	—	.01	—	.01	.03	.16	.12	—	.10
25—29	—	—	.01	—	.01	.11	.17	.06	—	.10
30—34	—	.02	—	—	.01	.08	.05	.07	.25	.08
35—39	.05	.05	.06	—	.05	.16	.18	.13	—	.14
40—44	.06	.06	.06	—	.06	.23	.33	.21	.62	.26
45—49	.19	.06	.07	—	.09	.39	.31	.23	.37	.29
50—54	.11	.25	.21	—	.18	.36	.50	.34	—	.37
55—59	.38	.41	.53	.28	.46	.38	.41	.34	.57	.38
60—64	.47	.58	.60	1.09	.58	.90	.87	.29	.36	.57
65—69	.86	.87	.76	.47	.80	.53	.64	.61	.94	.61
70—74	1.61	.96	.55	.67	.88	.38	.96	.51	—	.58
75—79	.83	.52	.62	1.30	.65	.50	1.30	.62	1.30	.78
80—	—	.75	.08	—	.23	1.39	.38	1.49	—	1.17
WOMEN										
0— 4	—	—	—	—	—	—	—	.03	—	.02
5— 9	—	—	—	—	—	.06	.05	.01	—	.03
10—14	—	—	—	—	—	.08	.08	.09	.16	.09
15—19	—	—	—	—	—	.04	.12	.03	—	.05
20—24	.03	—	—	—	.01	.03	.17	.08	—	.09
25—29	.02	—	—	.11	.01	.05	.11	.10	.11	.09
30—34	—	.02	—	—	.01	.09	.18	.09	.24	.13
35—39	.02	.02	.03	—	.03	.05	.05	.12	—	.08
40—44	.02	.05	.05	—	.04	.12	.36	.25	—	.23
45—49	.13	.11	.14	.19	.13	.16	.25	.29	.56	.26
50—54	.30	.35	.15	.22	.25	.30	.38	.19	—	.26
55—59	.41	.37	.30	—	.34	.38	.37	.48	.56	.42
60—64	.55	.59	.36	.71	.48	.47	.29	.54	.35	.45
65—69	.62	.66	.57	1.36	.63	.29	.61	.54	.91	.50
70—74	.59	.89	.30	1.34	.57	.39	.69	.56	.67	.55
75—79	.53	.75	.26	—	.46	.74	.53	.60	—	.60
80—	.84	.42	.33	—	.48	.84	.70	.41	—	.59

SMOKING HABITS OF PATIENTS WITH PAPILLOMA OF URINARY BLADDER

By JOHANNES CLEMMESEN, KNUD LOCKWOOD and ARNE NIELSEN

On the analysis of the material of Cancerregisteret for the years 1943 to 1953 inclusive (Clemmesen & Nielsen, 1956) it was discovered that papillomata of the urinary bladder, benign and malignant together, showed a steady increase in rates among men in the Danish Capital. In provincial towns and rural areas a less pronounced increase occurred among men during the years 1951 to 1953, but its significance seemed doubtful. Among women, no increase was observed for bladder tumours. Following a thorough comparison with rates for other urinary organs, and further analyses the authors concluded that the observed increase must be considered as real and due to an increase in the number of cases.

This pattern of increase showed a strong resemblance to the increase in rates for bronchial carcinoma, beginning about 1930 among men in Copenhagen, and spreading to provincial towns and rural areas eight and ten years later, which was striking, not only to ourselves, but also to

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interested colleagues following our publications (G. Bierring, 1955), and it was at once decided to start on the inquiry reported later in this paper. At the same time we compared Danish mortality rates at various ages for carcinoma of the bladder with those of other countries (Clemmesen, Nielsen & Lockwood, 1957). It appeared that the Danish curve for mortality rates took approximately the same course as curves for Australia, Canada, England & Wales, Italy, Netherlands, Scotland, and particularly the United States, while contrarily Japan, New Zealand, Norway and Sweden showed considerably lower rates of mortality than Denmark. Incidence rates for Copenhagen, the Danish capital, ran considerably higher than any of the mortality curves, and it should be pointed out that because of the accessibility to therapy of bladder papillomata at the benign stage the differences between nations with regard to therapeutic efficiency may influence figures for deaths from vesical carcinoma considerably. On the other hand, studies of endemiological character with a view to etiology statistics should comprise both benign and malignant papillomata.

For such reasons a comparison of mortality rates between countries must be taken with reservation, as far as bladder tumours are concerned, but it does seem worth while noticing that rates for Sweden and Norway, so similar to Denmark in most ways, are strikingly lower than those for the latter country.

Other studies on the present subject were however carried out simultaneously and independantly.

Holsti & Ermala (1955) for 140 consecutive days swabbed the lips and oral cavity of 60 albino mice of mixed known strain with tobacco tar. After an observation period of 12 months a benign papillomatosis had developed in 35 mice or 87.5 per cent of the animals surviving while malignant papilloma had appeared in six.

Lilienfeld, Levin & Moore (1956) analysed retrospectively the clinical records from the Roswell Park Memorial Institute of 321 white patients, aged 45 years or more, admitted from 1945 to 1955, and with a history of tobacco use.

Lilienfeld et al. concluded after various computations that a significantly larger proportion of men with urinary bladder cancer smoked cigarettes than did other classes of patients chosen for comparison. This association was limited to those who gave a history of having smoked for 30 years or more and was of a lower degree than that found in the case of lung cancer. For women with bladder cancer no association was found. It is strongly emphasized by the authors that their analyses require confirmation by similar investigations elsewhere.

Denoix & Schwartz (1956) inspired by the findings of Holsti & Ermala enquired

Table I.
Age-Adjusted Percentage of Men Aged Forty-Five Years and Over with History of Tobacco Use, by Class of Patient.
(Lilienfeld, Levin & Moore).

Class of Patient	No. of patients	Any type of tobacco	Cigarettes only	Cigarettes alone and ind combination with other type of tobacco	Any type other than cigarettes
Bladder Cancer.	321	84.7	48.7	61.4	23.2
Benign Bladder Conditions	39	77.9	32.8	37.1	40.8
No disease	337	70.8	35.8	44.1	26.7
Prostate Cancer	287	77.8	32.6	42.3	36.1
Lung Cancer ..	306	92.0	64.9	82.9	9.1

60 patients with malignant tumour of the urinary bladder, and groups of the same size with cancer of lung, of superior respiratory system, of nonmalignant diseases and a healthy group of persons. They found 95 per cent cigarette smokers among patients with bladder cancer against respectively 87 and 88 among noncancerous and healthy persons. While this difference was not significant it was found that bladder cancer patients smoked an average of 15,1 cigarettes daily against 11.7 among noncancerous and 12.1 among healthy which difference was significant ($p = 0.02$), and the per cent of inhalers were respectively 55 for bladder tumours and 30 (misprint?) and 38 for the other groups with a significant difference ($p = 0.03$).

MATERIAL

In planning the investigation into the causes of the increase of vesical papilloma among men in Copenhagen we paid full attention both to the occupational factors which for many years have been the best verified etiological feature of this disease, and to the possible significance of to-

Table 2.
Annual Consumption of Tobacco in Denmark per Inhabitant.

Year	Pieces		Kilogrammes	
	Cigars	Cigarrillos	Cigarettes	Smoking tobacco
1943	29	72	277	0.43
1944	29	76	330	0.46
1945	34	83	288	0.35
1946	75	116	524	0.64
1947	84	106	574	0.66
1948	92	114	635	0.74
1949	91	95	825	0.60
1950	90	94	938	0.59
1951	66	98	809	0.56
1952	49	125	895	0.59
1953	48	137	899	0.59
1954	47	141	870	0.60

For earlier years see: Clemmesen et al. 1953.

Table 3.

Patients with Bladder Papilloma

	Admitted in hospital København Frederiksberg		
	Men	Women	Total
1943 (and earlier)	10	3	13
1943	2	1	3
1944	5	1	6
1945	6	2	8
1946	11	1	12
1947	6	5	11
1948	15	5	20
1949	23	3	26
1950	20	8	28
1951	25	6	31
1952	34	10	44
1953	29	11	40
1954	50	12	62
1955	31	17	48
1956 (part)	15	2	17
Total	282	87	369

bacco smoking, as well as to a number of other possibilities. A detailed report of this study will be presented by one of us (L), when a sufficient number of control persons have been inquired. However, on the special question of tobacco smoking a valuable control material is already in being, established by the Danish Morbidity Survey of 1950, and previously treated by Hamtoft & Marie Lindhardt, 1955, 1956, kindly put at our disposal by the Director of Health Statistics, Miss Lindhardt.

Our first step was to organize an inquiry among all patients notified to the Danish Cancer Registry as suffering from vesical papilloma, whether benign or malignant, from its start and up to 1956, March 1, and alive at the time of inquiry. The distribution of cases according to year of first admission in hospital is given in Table 3. Through the Chief Surgeons of the hospital departments in question, covering the City of Copenhagen and the Borough of Frederiksberg, patients were asked for an appointment in their home, and the interviewer was introduced. Between March, 1, 1956 and November 30, 1957, 236 men and 74 women were interviewed by Dr. Lockwood and, for practical reasons, 47 men and 12 women by another of us (C) according to the same procedure. In 28 cases the patient had to be approached more than once, although usually not many times. Thirty-one cases had to be discarded for lack of response, while in 122 cases the patient had died or could not be traced.

The impression prevailing from our visits is one of gratitude and confidence of patients towards the hospital staffs, combined with full understanding of the nature of our study, as far as its general scope was concerned, and of readiness to assist. The lurking fear haunting most patients that their papilloma should develop into cancer induced us to avoid public discussion on the increase in incidence of bladder tumours, until it would be possible to advise on its possible causes. We have continuously assured patients that both benign and malignant papillomata were included in the study, and it may also be added that a possible relationship between tobacco smoking and bladder papilloma had not been debated in public in Denmark up to the present publication.

The original control material provided through Hamtoft & Lindhardt's survey of Danish smoking habits contains valuable details on kind of tobacco consumed of which we have taken advantage in the following. Also the regional subdivision which could be worked out on the basis of the records was of importance, because our material was limited to the municipalities of Copenhagen and Frederiksberg, while the Borough of Gentofte — the wealthier part of Greater Copenhagen — as demonstrated by Clemmesen, A. Nielsen & E. Jensen (1953) shows a rate for bronchial carcinoma of only 66 per cent of the Copenhagen average, against 107 for Frederiksberg, so that some difference in smoking habits might be expected.

The National Morbidity Survey's sample on smoking habits had been collected during two periods, namely August 1952 to April 1953, and January to April 1954, covering respectively 11,492 and 5,453 men and 11,800 and 5,273 women, and figures from both materials will appear in the following, although for more detailed analysis we have preferred the larger material dating from 1952—53. Some difference between the two materials with regard to smoking habits was observed by Hamtoft & Lindhardt who ascribed them to the effect on the public of the information on the association between cigarette smoking and bronchial carcinoma, given first time in Denmark in October 1952, at the annual meeting of the Cancer League. It will appear that the development in Copenhagen-Frederiksberg does not seem to have followed the general Danish trend. In this region no increase in non-smokers was observed and no decrease in the smoking of cigarettes, but, as it appears from our tables the total consumption decreased during the year in question, so that we shall be on the safe side in using the material for 1952—53.

Hamtoft & Lindhardt point to the difference of about 20 per cent between an estimate for whole Denmark based on their results, and the higher figures reported by official accounts on the sale of revenne labelled tobacco. The two authors emphasize that persons inquired will correctly base their estimate on the average daily consumption, leaving occasions of festivity out of consideration, and besides they assume a general tendency to underestimate consumption of any kind. The present authors have not been aware of any conscious tendency among patients to belittle their consumption of tobacco, although this possibility naturally was always in the mind of the interviewer. We are inclined to accept the

Table 4 a—d.

Danish Morbidity Survey 1952–53

Smoking Habits København - Frederiksberg

Age	Persons inquired	No inform.	Non-smokers	MEN PREFERRING Cigarettes	Cigars	Cigarillos	Pipe	Total number of smokers	Persons inquired	No inform.	Non-smokers	WOMEN PREFERRING Cigarettes	Cigars	Cigarillos	Pipe	Total number of smokers
Under 20	159	1	54	75		1	28	104	156	2	91	62		1		63
20—29	463	1	77	230	4	5	146	385	583	1	217	358	1	5	1	365
30—39	574	2	70	294	25	46	137	502	611		237	346	1	27		374
40—49	499		69	209	39	62	120	430	507	1	242	197	2	65		264
50—59	340		61	102	53	58	66	279	378		195	88	4	91		183
60—69	243		53	34	37	44	75	190	303		197	39	3	64		106
70—79	125		38	4	19	21	43	87	157	2	110	7	4	34		45
80—	25		11		5	1	8	14	31	1	25	2		3		5
Total	2428	4	433	948	182	238	623	1991	2726	7	1314	1099	15	290	1	1405

Age	MEN PREFERRING CIGARETTES: Pure cigarette smokers by total consumption grams per day -5	6-15	16-25	26-	Total	Mixed cigarette smokers by total consumption grams per day -5	6-15	16-25	26-	Total	WOMEN PREFERRING CIGARETTES: Pure cigarette smokers by total consumption grams per day -5	6-15	16-25	26-	Total	Mixed cigarette smokers by total consumption grams per day -5	6-15	16-25	26-	Total
Under 20	29	37		1	67		2	5	1	8	30	30	1	1	62					
20—29	32	104	26	5	167	1	26	27	9	63	144	205	8	1	358					
30—39	30	113	74	13	230	1	19	35	9	64	134	191	18	1	344		2			2
40—49	14	99	45	7	165	1	12	23	8	44	76	100	16		192	2	2	1		5
50—59	10	44	32	3	89	1	5	5	2	13	51	32	3	1	87		1			1
60—69	11	12	5		28		3	2	1	6	27	12			39					
70—79	3	1			4						6	1			7					
80—											2				2					
Total	129	410	182	29	750	4	67	97	30	198	470	571	46	4	1091	2	5	1		8

Age	MEN PREFERRING CIGARILLOS: Pure cigarillos smokers -5	6-15	16-25	26-	Total	Mixed cigarillos smokers -5	6-15	16-25	26-	Total	WOMEN PREFERRING CIGARILLOS: Pure cigarillos smokers -5	6-15	16-25	26-	Total	Mixed cigarillos smokers -5	6-15	16-25	26-	Total
Under 20								1		1	1				1					
20—29	1				1			2	2	4	1	1	1	1	4		1			1
30—39	3	10	8	5	26		5	7	8	20	4	13	7	2	26		1			1
40—49	2	16	11	10	39		6	9	8	23	9	32	14	9	64		1			1
50—59	3	13	10	10	36		4	11	7	22	23	40	16	11	90	1				1
60—69	5	14	9	6	34	1	6	2	1	10	16	37	5	2	60	2			2	4
70—79	2	11	1		14		3	2	2	7	10	19	3	1	33	1				1
80—		1			1						1	2			3					
Total	16	65	39	31	151	1	24	34	28	87	65	144	46	26	281	4	3		2	9

Age	MEN PREFERRING CIGARS: Pure cigar smokers -5	6-15	16-25	26-	Total	Mixed cigar smokers -5	6-15	16-25	26-	Total	MEN PREFERRING PIPE: Pure pipe smokers -5	6-15	16-25	26-	Total	Mixed pipe smokers -5	6-15	16-25	26-	Total
Under 20											4	7			11		13	4		17
20—29	1	1			2				2	2		45	7	2	54		55	30	7	92
30—39		5	2	6	13		5	3	4	12	1	37	12	6	56	1	38	32	10	81
40—49	1	8	5	6	20	1	2	6	10	19	2	42	10	8	62		17	29	12	58
50—59	2	12	9	13	36		4	7	6	17		18	5	7	30		14	21	1	36
60—69	2	7	4	5	18		3	5	11	19	3	38	7	4	52	1	10	8	4	23
70—79	3	5	2	2	12		1	2	4	7	4	23	1	2	30	1	10	1	1	13
80—	1	1		1	3		1	1		2		6			6		1	1		2
Total	10	39	22	33	104	1	16	24	37	78	14	216	42	29	301	3	158	126	35	322

	WOMEN PREFERRING CIGARS										WOMEN PREFERRING PIPE									
Total	2	5		6	13		1	1				1			1					

view of Hamtoft & Lindhardt and would primarily assume that our papilloma patients have been subject to the same errors as the persons inquired for the National Morbidity Survey, which assumption we find supported by a number of similarities between the two materials appearing from Table 5.

According to the principles once adopted by Hamtoft & Lindhardt all persons who admitted to smoking at all were designated as smokers. The few who did not state whether they smoked or not have been listed under "no information" in our tables. Subdivision into the groups cigarette smokers, pipe smokers etc. had

been made according to the greatest consumption, those smoking more than one form of tobacco being placed in one group only, but then with their total consumption. Where the consumption of different forms was equally high the survey classified them in the order: cigarettes, pipe, cigars and cigarillos. Persons who were smokers, but did not state the form of tobacco, were for males reckoned as pipe smokers and for females as cigarette smokers. Grouping the smokers according to the quantity smoked was carried out partly with reference to the tobacco-smoking investigations that have been made in other countries. The general rule was followed of reckoning a cigarette as containing 1 g, a cigarillo 4 g, and a cigar 7 g. Thus one cigarette would correspond to 1 g of pipe tobacco.

Table 3 gives a survey of the age distribution of normal persons inquired about their smoking habits and grouped according to preferred type of tobacco, including socalled "mixed smokers". Because of the steady increase in tobacco consumption in Denmark during the last decades, except during World War II, illustrated in Table 2, there is no risk that the spreading of our patients with bladder papilloma over the years should tend to give higher figures for tobacco consumption than those given for the average population in Copenhagen 1952—53 in Table 4.

In order to leave no doubt about Danish smoking habits in the capital we have in Tables 4, a, b, c, d, reported consumption figures for smokers preferring the various categories of tobacco according to age and sex, separately for "pure smokers" and for "mixed smokers".

Danish figures will differ from those of many other countries in comprising a relatively high number of cigar smokers. Also the number of women smoking cigarillos may be characteristic.

In Table 5 results are given for two major age groups, respectively of 20 to 59 years and for 60 years and over, each age group adjusted for ten year subgroups. The first column gives numbers of patients from the inquiry, and the following two the corresponding numbers computed on the basis of the material from the Danish Morbidity Survey for each of its two periods examined, all columns specified according to preferred kind of tobacco.

It appears that the figures for non-smokers among patients fall far below those for the normal population in both of the major age groups. For smokers preferably of cigarettes numbers are higher among male patients than in the population 1952/53. For the younger age group the difference can be regarded as certain, and the same applies to cigar smokers. For cigarillos there seems to be a similar, although not very pronounced tendency for men, and a stronger trend for women. Figures for pipe smokers show no certain tendency.

A survey of the risk in relation to increasing quantities for total tobacco consumption worked out on the basis of the same material shows a solid difference between patients and normal persons at doses exceeding 16 g a day. This

Table 5.

Bladder Papilloma Patients Compared with Normal Population.
København - Frederiksberg.

	MEN						WOMEN					
	20—59 years Age-adjusted			60 years and over Age-adjusted			20—59 years Age-adjusted			60 years and over Age-adjusted		
	Patients inquired	Computed number 1952/53	1954	Patients inquired	Computed number 1952/53	1954	Patients inquired	Computed number 1952/53	1954	Patients inquired	Computed number 1952/53	1954
Main kind of tobacco	*According to Preferred Kind of Tobacco*											
Non-smokers	1	23.5	22.0	25	34.8	30.0	10	14.6	14.1	39	39.5	40.9
Cigarettes	66	51.8	53.4	18	14.1	19.6	8	8.2	8.5	4	5.4	4.9
Cigars	26	17.5	12.4	24	21.2	16.9	1	0.2	0.1	0	0.8	—
Cigarillos	22	21.1	20.1	30	23.2	34.8	10	6.0	6.1	15	11.9	12.2
Pipe	30	31.1	36.8	40	43.7	34.8	0	—	0.2	0	—	—
No inform.	—	0.0	0.3	—	—	0.8	—	0.0	0.0	—	0.4	—
Total	145	145.0	145.0	137	137.0	136.9	29	29.0	29.0	58	58.1	58.0
Total consumption of tobacco	*According to Quantities Consumed*											
Non-smokers	1	23.5	22.0	25	34.8	30.0	10	14.6		39	39.5	
0— 5 g	5	6.8	18.4	2	12.9	26.5	3	5.6		3	7.8	
6—15 g	30	52.9	77.0	37	54.4	54.9	8	6.3		10	8.8	
16—25 g	47	41.8	20.8	25	19.2	19.2	4	1.6		5	0.9	
26 g and more	62	20.0	6.5	48	15.7	5.0	4	0.9		1	0.6	
No inform.	—	0.0	0.3	—	—	1.5	—	0.0		—	0.4	
Total	145	145.0	145.0	137	137.0	137.1	29	29.0		58	58.0	
χ^2		120.8			85.7			8.55			6.11	
Degrees of freedom		4			4			2			2	
Prohability less than		0.1 per cent			0.1 per cent			5.0 per cent			5.0 per cent	

Table 6.
City of Copenhagen and Borough of Frederiksberg.

Amount of consumption	Type of smoking of patients inquired and age-adjusted distribution of controls for 1952/53							
	Cigarettes only		Cigars only		Cigarillos only		Pipe only	
	Pat.	Cont. 1952/53	Pat.	Cont. 1952/53	Pat.	Cont. 1952/53	Pat.	Cont. 1952/53
0— 5 g.	4	11.3	0	2.1	2	3.0	1	2.5
6—15 g.	19	29.5	1	6.3	5	11.8	23	27.1
16—25 g.	26	16.6	0	3.6	6	6.3	11	3.6
26— g.	10	1.8	16	5.0	13	4.8	2	3.8
Total	59	59.2	17	17.0	26	25.9	37	37.0
χ^2	27.1		12.9		18.1		5.30	
Degree of freedom	2		1		2		1	
Probability less than	0.1 per cent		0.1 per cent		0.1 per cent		5.0 per cent	

suggests that the carcinogenic effect on the bladder mucosa may require a consumption of large quantities.

In table 6 giving consumption figures for "pure smokers" we find a clear excess of smokers of cigarettes, cigars, and cigarillos among male patients with bladder papilloma, while figures for pipe smokers scarcely show any definite trend. The numbers of women are too small for analysis.

CONCLUSIONS

The increase in incidence of bladder papilloma observed among men in Copenhagen is parallel to the increase in mortality and incidence of bronchial carcinoma, although taking place at a lower level.

Male patients with bladder papilloma in Copenhagen-Frederiksberg show lower numbers of non-smokers than do normal persons according to the sample study by the Danish Morbidity Survey. Correspondingly, a higher proportion of pure smokers among the patients show a high consumption of cigarettes, of cigars and of cigarillos, than the average men. Similar trends, but less pronounced can be traced among the limited number of women affected by bladder papilloma. Our observation is in harmony with the limited studies previously published on this subject.

From a biological point of view this observation goes well with the observation by numerous authors that persons, and nations, with a high consumption of cigarettes show higher rates for bronchial carcinoma than others. According to our results smokers of cigars and cigarillos participate in the increased risk of bladder papilloma.

However, even in Copenhagen, which, so far, seems to show the highest rates for incidence of bladder papilloma, the incidence rate for this disease is relatively low up to now, although the absence of industrial bladder papillomata may contribute to this state of affairs. It would therefore probably be unjustified to warn against smoking only on the basis of the association between tobacco consumption and this disease.

The very rarity of bladder papilloma suggests the existence of unknown "conditioning factors" or some disposition of the person affected, besides excessive smoking of tobacco, but we know that persons once befallen with bladder papilloma and thus proven responsive to a causative agent will often show recurrences, and often develop malignant change. Such changes may be produced by continuous exposure to causative factors, and the removal of at least some of these may be decisive for the fate of the patient. We would therefore advise doctors that such patients should, if possible, be dissuaded from the smoking of tobacco, or at any rate restrict themselves to the use of a pipe.

We are of opinion that further studies on this subject will give valuable information.

SUMMARY

A preliminary report on an inquiry among patients with bladder papilloma in Copenhagen, where rates of incidence for this disease in on the increase. 369 patients have been interviewed, and show a larger proportion of smokers, and of heavy pure smokers of cigarettes, cigars, and cigarillos than the normal population. It is suggested that it may reduce the risk of recurrences and of malignancy if patients with bladder papilloma abstain from smoking.

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